1 H, C-5 H), 7.96 (br s, 2 H, NH_2); IR (KBr) 3370, 3265, 3215, 2230, 1620 cm^{-1}.

Anal. Calcd for $C_8H_{10}N_4O_3$: C, 45.71; H, 4.80; N, 26.66. Found: C, 45.38; H, 4.80; N, 26.42.

Method B. A solution of 0.50 g (2 mmol) of aminomalononitrile tosylate in 3 mL of methanol was cooled in an ice bath and a solution of 0.27 g of crude **41** in 1 mL of methanol added in one portion. TLC (10% MeOH, 90% $CHCl_3$) examination of the resulting dark red solution indicated that a complex mixture of products had formed, but comparison with authentic **42** indicated its presence in the reaction mixture. This reaction was not investigated further.

2-Amino-3-cyano-5-(dimethoxymethyl)pyrazine (4). A solution of 1.48 g (5 mmol) of *O*-tosyloximinomalononitrile in 50 mL of anhydrous ethyl ether was cooled to −20 °C under nitrogen and a solution of 1.71 g (10 mmol) of 3,3-dimethoxy-1-pyrrolidinopropene in 12 mL of ether was added dropwise. The mixture was then allowed to warm to 0 °C and kept at 0 °C for 1 h. Saturated methanolic ammonia (20 mL) was then added and the resulting mixture kept at 0 °C for an additional h. The mixture was filtered and the filtrates were concentrated in vacuo to give a brown gum which was partitioned between 50 mL of ether and 25 mL of water. The layers were separated, the aqueous layer was extracted with ether (3 × 25 mL), and the combined ether extracts were dried ($MgSO_4$) and evaporated in vacuo to leave a brown oil in which crystals formed on standing. The product was filtered off and rinsed with cold toluene to give 0.23 g of light golden crystals, mp 94–95 °C (lit.[3] mp 91–93 °C), identical with authentic material. The filtrates were stirred overnight with activated carbon and concentrated to a small volume to give a second crop of 0.07 g (31% total yield).

2-Amino-3-cyanopyridine (44). A solution of 1.22 g (10 mmol) of (ethoxymethylene)malononitrile (Aldrich) in 10 mL of dry THF was cooled to −25 °C and a solution of 1.71 g (10 mmol) of **38** in 10 mL of THF added dropwise. The resulting solution was allowed to warm to 10 °C and 10 mL of saturated methanolic ammonia added. The reaction mixture was then stirred overnight with gradual warming to room temperature. The solvent was removed in vacuo, the residue was taken up in 25 mL of ethyl acetate and extracted with 25 mL of 1 N HCl, and the aqueous layer added carefully to 25 mL of saturated sodium bicarbonate. It was then extracted with methylene chloride (2 × 20 mL), the extracts were dried ($MgSO_4$) and evaporated under reduced pressure, and the residue was chromatographed (silica gel, ether) to give 0.020 g (1.7%) of a white solid, mp 129–130 °C (lit.[41] mp 131–133 °C), identical with an authentic sample of **44**.

Registry No. 3, 76282-54-7; **4**, 6440-77-3; **5**, 6342-56-9; **7**, 76282-55-8; **8**, 76282-56-9; **9**, 76282-57-0; **10a**, 76282-58-1; **10a**·2Na, 76282-59-2; **11**, 76282-60-5; **13**, 5098-14-6; **14**, 73198-29-5; **15**, 20893-01-0; **16**, 76282-61-6; **17**, 76282-62-7; **18**, 76299-37-1; **19**, 76299-38-2; **20a**, 672-81-1; **20b**, 123-06-8; **21**, 76282-63-8; **22**, 76282-64-9; **23**, 76299-39-3; **24**, 76282-65-0; **25a**, 94-09-7; **25b**, 76282-66-1; **25c**, 52407-60-0; **26a**, 76282-67-2; **28**, 76282-68-3; **29**, 76282-69-4; **30a**, 76282-70-7; **30b**, 76282-71-8; **31a**, 76282-72-9; **31b**, 76282-73-0; **32a** (isomer 1), 76282-74-1; **32a** (isomer 2), 76282-75-2; **33a**, 76299-40-6; **33c**, 76282-76-3; **34**, 76319-72-7; **36a** (isomer 1), 76282-77-4; **36a** (isomer 2), 76282-78-5; **36c**, 76282-79-6; **37a**, 76282-80-9; **38**, 76282-81-0; **41** (isomer 1), 76282-82-1; **41** (isomer 2), 76282-83-2; **42**, 76282-84-3; **44**, 24517-64-4; pyrrolidine, 123-75-1; nitrosyl chloride, 2696-92-6; guanidine, 113-00-8; 3-pyrrolidinoacrolein, 30545-31-4; N^2-acetyl-5-deaza-7-(diacetoxymethyl)pterin, 76282-85-4.

(41) Taylor, E. C.; Crovetti, A. J. *J. Org. Chem.* **1954**, *19*, 1633–1644.

Intramolecular 1,1-Cycloaddition of Nitrilimines as a Route to Benzodiazepines and Cyclopropa[*c*]cinnolines

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Received November 19, 1980

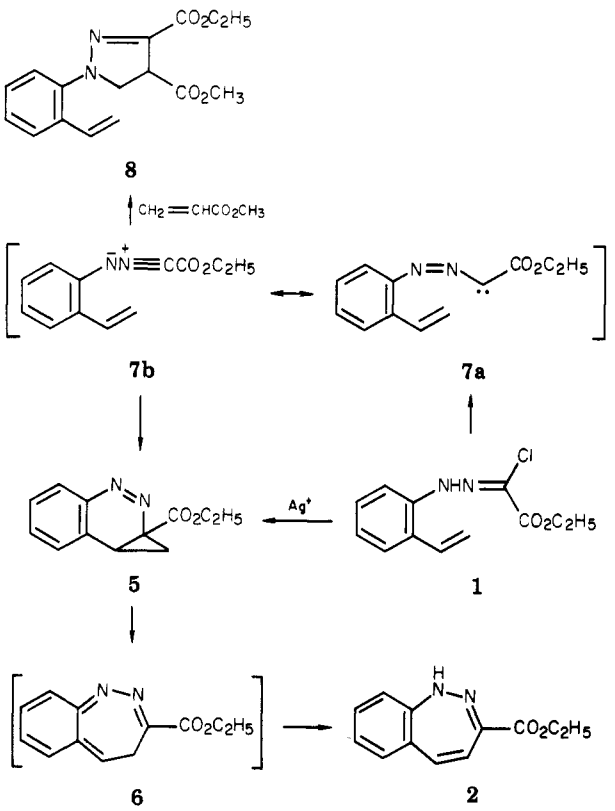
Treatment of *o*-vinylphenyl-substituted chloroglyoxylate phenylhydrazones with base leads to nitrilimines. These reactive 1,3-dipoles undergo intramolecular 1,1-cycloaddition with complete retention of configuration to give cyclopropa[*c*]cinnolines. When the nitrilimine was generated in the presence of an added dipolarophile, bimolecular 1,3-dipolar cycloaddition was the exclusive reaction observed. Thermolysis of the cyclopropa[*c*]cinnoline ring resulted in the formation of benzodiazepines. This thermal rearrangement is readily explicable in terms of an electrocyclic ring opening followed by a 1,5-sigmatropic shift of the transient ring-opened diazanorcaradiene intermediate. The ring-opened species can be trapped with added dipolarophiles to give 5-substituted 4,5-dihydrobenzodiazepines. Treatment of the homologous *o*-allylphenyl chlorohydrazone with base results in a 1,3-dipolar cycloaddition. With this system, the transition state for cycloaddition allows easy attainment of the parallel plane approach of the dipole and dipolarophile.

Nitrilimines are a long known and thoroughly investigated class of 1,3-dipoles.[1] Access to this group of dipoles can be realized by (a) treatment of hydrazonyl halides with base,[2] (b) thermal or photochemical decomposition of tetrazoles,[3,4] (c) photolysis of sydnones,[5] and (d) thermal elimination of carbon dioxide from 1,3,4-oxadiazolin-5-ones.[6,7] 1,3-Dipolar cycloaddition of this class of 1,3-dipoles has been widely investigated[8] and in many cases has led to the synthesis of a variety of interesting heterocyclic compounds,[9] some of which would be tedious to synthesize by other routes. The mechanism of the reaction of alkenes

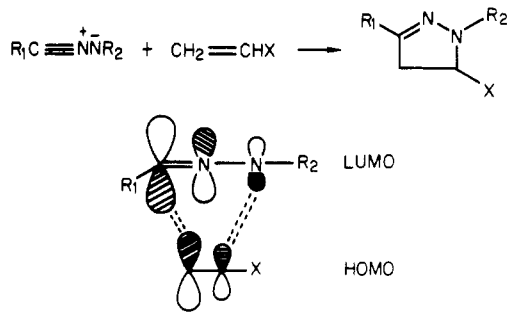
(1) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565, 633 (1963).
(2) R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, **17**, 3 (1962).
(3) R. Huisgen, M. Seidel, J. Sauer, J. W. McFarland and G. Wallbillich, *J. Org. Chem.*, **24**, 892 (1959); J. S. Clover, A. Eckell, R. Huisgen, and R. Sustmann, *Chem. Ber.*, **100**, 60 (1967).
(4) P. Scheiner and J. F. Dinda, Jr., *Tetrahedron*, **26**, 2619 (1970); P. Scheiner and W. M. Litchman, *J. Chem. Soc., Chem. Commun.*, 781 (1972).
(5) M. Marky, H. Meier, A. Wunderli, H. Heimgartner, H. Schmid, and H. J. Hansen, *Helv. Chim. Acta.*, **61**, 1477 (1978).
(6) C. Wentrup, A. Damerius, and W. Richen, *J. Org. Chem.*, **43**, 2037 (1978).
(7) A. Padwa, T. Caruso, and S. Nahm, *J. Org. Chem.*, **45**, 4065 (1980).
(8) R. Huisgen, R. Grashey, and J. Sauer in the "The Chemistry of Alkenes", S. Patai, Ed., Interscience, New York, 1964, p 806.
(9) A. Padwa, *Angew. Chem., Int. Ed. Engl.*, **15**, 123 (1976).

0022-3263/81/1946-1402$01.25/0

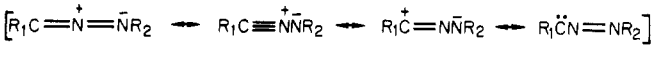
Scheme I



with nitrilimines has been the subject of intensive study and there now appears to be agreement that this is generally a concerted reaction in which the bonds to the two termini of the dipolarophile are formed at or about the same time.[10] The cycloadditions of simple nitrilimines with electron-rich dipolarophiles are LU (1,3-dipole)–HO (dipolarophile) controlled.[11-13] For conjugated dipolarophiles, both HO and LU interactions are important, but the greater difference in LU coefficients leads to a preference for 5-substituted Δ^2-pyrazolines.[12] With electron-deficient dipolarophiles the regioselectivity is reversed since the cycloaddition becomes HO (1,3-dipole)–LU (dipolarophile) controlled.

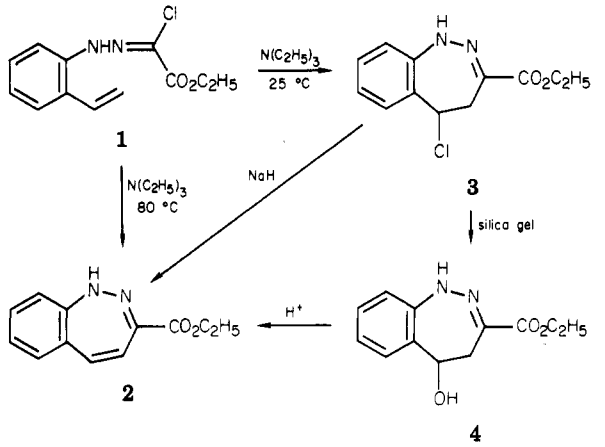


Among the possible geometric forms of a nitrilimine, a carbene structure can be envisaged which makes conceivable a 1,1-cycloaddition of this 1,3-dipole.[14,15] Recently, it has been shown that 1,1-intramolecular cycloaddition of nitrilimines can compete with the normal 1,3-addition when certain geometric constraints are imposed.[16,17] As a further consequence of our interest in this area,[18] we thought it worthwhile to determine whether additional examples of carbenoid activity of nitrilimines could be uncovered. In this paper we describe some of our efforts involving the generation and the chemistry of a number of nitrilimines containing unsaturation several atoms away from the dipole center.



Results and Discussion

As our first model we chose to investigate the intramolecular dipolar cycloaddition reaction of hydrazonyl chloride **1**. This material was prepared from *o*-vinylaniline through diazotization and coupling with the anion of 2-chloroacetoacetic ester. Treatment of hydrazonyl chloride **1** with triethylamine in benzene at 80 °C for 5 h gave a 91% yield of ethyl 1*H*-1,2-benzodiazepine-3-carboxylate (**2**), mp 107–108 °C, as the only detectable product. When

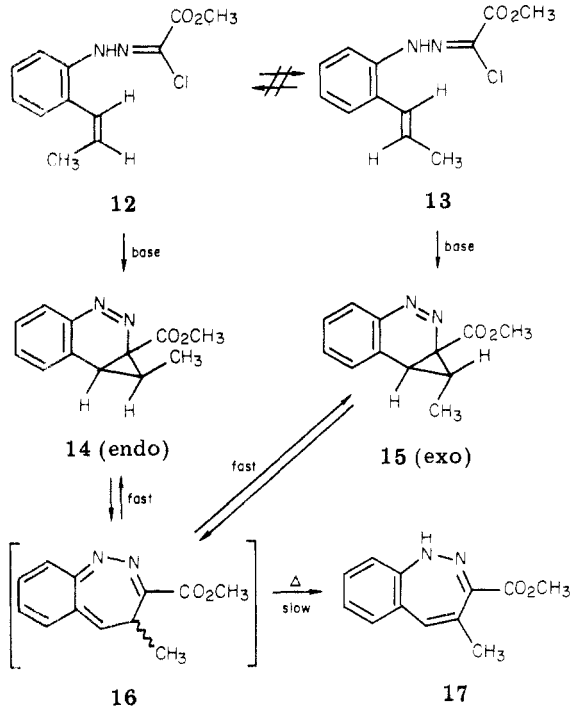


the reaction of **1** with triethylamine was carried out at room temperature, a new product was obtained whose structure was assigned as ethyl 4,5-dihydro-5-chloro-1*H*-1,2-benzodiazepine-3-carboxylate (**3**). This material was identified on the basis of its characteristic 100-MHz spectrum ($CDCl_3$) which showed a triplet at δ 1.31 (3 H, J = 7.0 Hz), a set of doublet of doublets at δ 3.02 (1 H, J = 17.0, 2.0 Hz), 3.87 (1 H, J = 17.0, 6.0 Hz), and 5.36 (1 H, J = 6.0, and 2.0 Hz), a quartet at δ 4.23 (2 H, J = 7.0 Hz), a multiplet at δ 6.8–7.3 (4 H), and a broad singlet at δ 10.0 (1 H). This structure was further supported by its ready conversion to benzodiazepine **2** on treatment with sodium hydride at 25 °C or with triethylamine in refluxing benzene. Attempts to purify **3** by thick-layer chromatography led to the isolation of the corresponding alcohol **4**. The acid-catalyzed dehydration of **4** also led to the formation of benzodiazepine **2**.

When the reaction of **1** was carried out in benzene at room temperature in the presence of silver carbonate and HMPA to precipitate the chloride salts, the only product obtained was 1*H*-cyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (**5**) in 92% yield. This product was identified on the basis of its characteristic 100-MHz NMR spectrum ($CDCl_3$) which showed a set of doublet of doublets at δ 0.11

(10) R. Huisgen, *J. Org. Chem.*, **41**, 403 (1976).
(11) I. Fleming, "Frontier Orbitals and Organic Chemical Reactions", Wiley, New York, 1976.
(12) K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc.*, **95**, 7301 (1973).
(13) K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973).
(14) P. Caramella and K. N. Houk, *J. Am. Chem. Soc.*, **98**, 6397 (1976).
(15) P. Caramella, R. W. Gandour, J. A. Hall, C. G. Deville, and K. N. Houk, *J. Am. Chem. Soc.*, **998**, 385 (1977).
(16) A. Padwa and S. Nahm, *J. Org. Chem.*, **44**, 4746 (1979).
(17) L. Garanti, A. Vigevami, and G. Zecchi, *Tetrahedron Lett.*, 1527 (1976); L. Garanti and G. Zecchi, *J. Chem. Soc., Perkin Trans. 1*, 2092 (1977).
(18) A. Padwa, S. Nahm, and E. Sato, *J. Org. Chem.*, **43**, 1664 (1978).

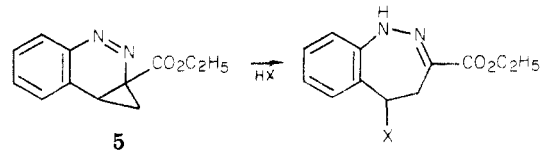
Scheme II



(1 H, J = 7.0 and 4.0 Hz), 2.75 (1 H, J = 9.0, 4.0 Hz), 3.11 (1 H, J = 9.0, 7.0 Hz), a triplet at δ 1.38 (3 H, J = 7.0 Hz), a quartet at δ 4.38 (2 H, j = 7.0 Hz), and a multiplet at δ 7.3–7.6 (4 H). Cyclopropa[c]cinnoline **5** was readily converted to benzodiazepine **2** on thermolysis at 80 °C. This thermal rearrangement is readily explicable in terms of an electrocyclic ring opening of **5** to **6** followed by a 1,5-sigmatropic shift of the transient ring-opened species (Scheme I). The conversion of **5** to **6** is closely related to the thermal valence tautomerization of norcaradienes to cycloheptatrienes.[19-22] The formation of structure **5** (and/or **2**) could be markedly suppressed when hydrazidoyl chloride **1** was treated with base in the presence of excess methyl acrylate. In addition to benzodiazepine **2**, the expected 1,3-dipolar cycloadduct **8** was isolated in 38% yield. Clearly nitrilimine **7** is an intermediate in this reaction and **5** arises by intramolecular 1,1-cycloaddition of the transient nitrilimine with the neighboring double bond. Analogous results have been reported by Garanti and coworkers with related systems.[17]

In the presence of acidic methanol, cyclopropa[c]cinnoline **5** was rapidly converted to 5-methoxy-4,5-dihydro-1*H*-1,2-benzodiazepine (**9**). A similar transformation occurred on treatment of **5** with ethanol or acetic acid. The identity of the products was assigned on the basis of their straightforward spectral properties (see Experimental Section).[23]

In order to probe the stereochemical aspects of the intramolecular 1,1-cycloaddition reaction, we have investigated the base-induced reactions of the *cis*- (**12**) and *trans*- (**13**) methyl-substituted chlorohydrazones (Scheme II).



5

3, X = Cl
9, X = OCH_3
10, X = OC_2H_5
11, X = $OCOCH_3$

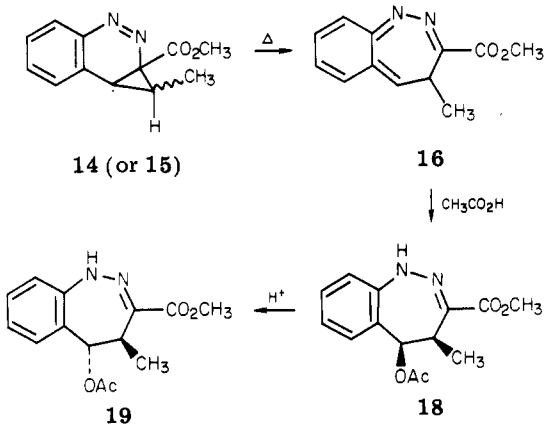
Reaction of *cis*-chlorohydrazone **12** with silver carbonate for 48 h produced a 3:1 mixture of the *endo*- (**14**) and *exo*-cyclopropa[c]cinnolines (**15**). This equilibirum mixture was fractionally crystallized to give a pure sample of the endo isomer **14**: mp 98–99 °C; NMR ($CDCl_3$, 100 MHz) δ 0.33 (d, 3 H, J = 6.5 Hz), 2.94 (dq, 1 H, J = 9.0, 6.5 Hz), 3.30 (d, 1 H, J = 9.0 Hz), 3.95 (s, 3 H), 7.3–8.3 (m, 4 H). The NMR of the exo isomer (**15**) 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 appearance of the methyl group in **14** (δ 0.33) at high field relative to the methyl group in **15** (δ 1.51) is compatible with the anisotropic shielding of this group by the π system of the diazabicycloheptene ring.[24] In addition, the magntitude of the proton coupling constant with **14** (J = 9.0 Hz) implies *cis*-cyclopropyl vicinal coupling[25,26] and fixes the methyl group in the endo position.

The same epimeric mixture of isomers was produced on heating *trans*-chlorohydrazone **13** with silver carbonate at 80 °C for 2 h. It should be noted, however, that when the reaction of **12** (or **13**) was carried out for short periods of time, the cycloadditions were completely stereospecific. Thus, treatment of **12** with base for 3 h afforded **14** as the exclusive product. Similarly, chlorohydrazone **13** gave cycloadduct **15** as the sole product after being stirred with base for 24 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., **14**) 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 **17** 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 **16** as a transient intermediate. This species undegoes a ring flip and reclosure at a faster rate than it undergoes a 1,5-sigmatropic hydrogen shift.

In order to obtain additional support for the mechanism proposed for the conversion of the cyclopropa[c]cinnoline ring to benzodiazepine **17**, we decided to determine whether diazanorcaradiene **16** could be intercepted with an external nucleophile. We found that treatment of **14** with acetic acid gave rise to a single product in high yield. This same material was also obtained from the exo isomer **15**. The C^{13} NMR showed a signal at 142.6 ppm which is clearly consistent with dihydrobenzazepine **18**. Further heating of this compound in toluene with a trace of acid

(19) J. A. Berson and M. R. Willcott, *J. Am. Chem. Soc.*, **88**, 2494 (1966); J. A. Berson, P. W. Grubb, R. A. Clark, D. R. Hartter, and M. R. Willcott, *ibid.*, **89**, 4076 (1967).
(20) G. Maier, *Angew. Chem.*, **79**, 446 (1967).
(21) A. Steigel, J. Sauer, D. A. Kleier, and G. Binsch, *J. Am. Chem. Soc.*, **94**, 2770 (1972).
(22) H. E. Zimmerman and W. Eberbach, *J. Am. Chem. Soc.*, **95**, 3970 (1973).
(23) It should be noted that Garanti and Zecchi have reported that the cyclopropa[c]cinnoline ring undergoes an acid-catalyzed ring opening; see L. Garanti and G. Zecchi, *J. Chem. Soc., Perkin Trans. 1*, 1195 (1979).
(24) A. Padwa and E. Glazer, *J. Am. Chem. Soc.*, **94**, 7788 (1972).
(25) W. G. Dauben and W. T. Wipke, *J. Org. Chem.*, **32**, 2976 (1967).
(26) M. Schneider and R. J. Crawford, *Can. J. Chem.*, **48**, 628 (1970).

resulted in epimerization to the thermodynamically more stable trans isomer. The preferential formation of the cis isomer **18** can be attributed to kinetic attack of the acetate group onto structure **16** from the least hindered position.

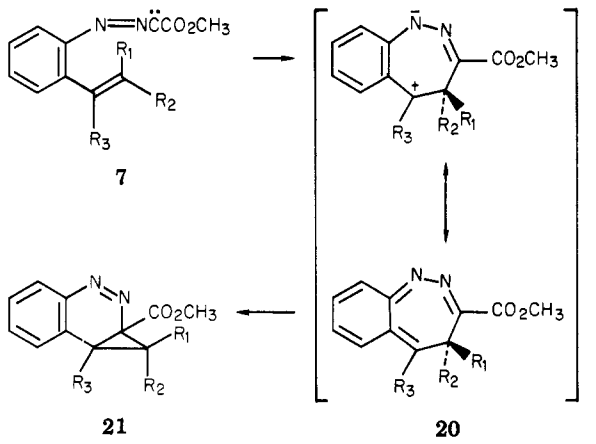


14 (or **15**) **16** **19** **18**

The primary spatial requirement for intramolecular dipolar cycloaddition is that the distance between the two reacting centers should be sufficiently short so that effective three-center overlap of the 1,3-dipole with the dipolarophile occurs. For concerted 1,3-dipolar cycloaddition to take place, the atoms of the dipolarophile should be arranged in such a way as to allow their p orbitals to lie in a plane parallel to the plane of the 1,3-dipole.[1] Recent MO calculations by Houk and Caramella suggest that nitrilimine is a flexible 1,3-dipole which can adapt its geometry according to the nature of the reaction.[14,15] Electrophilic reagents would tend to a favor a planar nitrilimine structure possessing a relatively high-lying HOMO, whereas nucleophilic reagents will promote the bent azocarbene-like form, which possesses a low-lying LUMO. Inspection of molecular models of the *o*-vinylphenyl-substituted chlorohydrazones indicates that the normal "two-plane" orientation approach of the nitrilimine and the vinyl π system is impossible as a result of the geometric restrictions imposed on the system. Consequently, the normal mode of 1,3-dipolar cycloaddition does not occur here. With this system, attack by the double bond is constrained to occur perpendicular to the plane of the nitrilimine. The 1,1-cycloaddition is initiated by interaction of the terminal carbon of the vinyl group with the second LUMO of the nitrilimine. The second LUMO of the dipole is perpendicular to the nitrilimine plane and presents a large vacancy of C_1 of the dipole for attack by the terminius of the neighboring double bond, without the possibility of simultaneous bonding at the N_3 nitrogen. In fact, the HOMO and second LUMO of the bent nitrilimine bear a strong resemblance to the HOMO and LUMO of a singlet carbene. Carbenes, of course, are known to react rapidly with alkyl-substitued double bonds.[27]

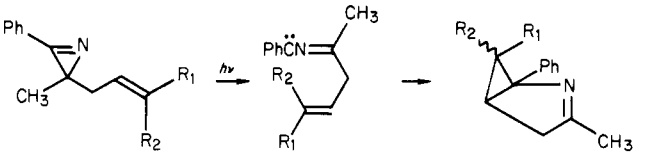
The results with chlorohydrazines **12** and **13** indicate that complete retention of stereochemistry about the π system has occurred in the 1,1-cycloaddition reaction. Since our original report, several additional examples of the 1,1-cycloaddition proceeding via retention of stereochemistry have been reported by Garanti and Zecchi.[28] This stands in marked contrast with the stereochemical course of the intramolecular 1,1-cycloaddition of the closely related nitrile ylide system. The lack of stereospecificity and formation of mixtures of isomeric azabicyclohexenes in the previously reported examples of 1,1-cycloaddition

Scheme III



7 **21** **20**

of allyl-substituted nitrile ylides[29-33] suggested that the reaction occurs by a stepwise addition of the 1,3-dipole onto the neighboring double bond.[34]

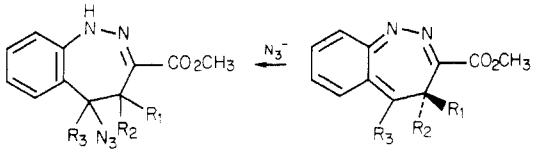


Reasonable mechanistic options for the 1,1-cycloaddition of the nitrilimine derived from ethyl chloroglyoxylate *o*-vinylphenyl)hydrazone include a concerted pathway or a stepwise process. The concerted path would parallel the stereospecific addition of singlet carbenes to olefins.[35] Stepwise nucleophilic attack of the terminal double bond on the electron-deficient carbon atom of nitrilimine **7** 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-electrocyclization process. This reaction is similar to that involved in the rearrangement of oxepins to benzene oxides[36] and that of diazocycloheptatrienes to diazanorcaradienes.[37] As long as the 1,6-electrocyclization reaction is fast relative to ring flipping, the 1,1-cycloaddition will proceed with retention of configuration.

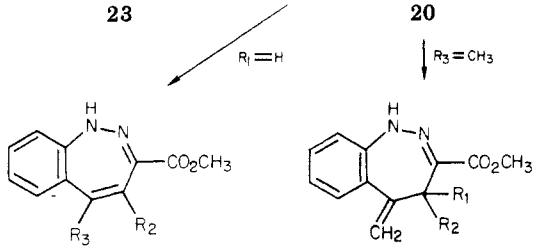
Supporting evidence for the involvement of **20** as a transient species in the formation of the cyclopropacinnoline ring is provided by the fact that **20** can be trapped with added nucleophiles such as acetate or azide anion.[38,39] Rearrangement of **20** directly to the benzodiazepine ring has also been found.[23] The formation of

(27) W. Kirmse in "Carbene Chemistry", Academic Press, New York, 1964.
(28) L. Garanti and G. Zecchi, *J. Heterocycl. Chem.*, **16**, 377 (1979).
(29) A. Padwa and P. H. J. Carlsen, *J. Am. Chem. Soc.*, **98**, 2006 (1976); *ibid.*, **99**, 1514 (1977).
(30) A. Padwa, A. Ku, A. Mazzu, and S. I. Wetmore, *J. Am. Chem. Soc.*, **98**, 1048 (1976).
(31) A. Padwa, P. H. J. Carlsen, and A. J. Ku, *J. Am. Chem. Soc.*, **99**, 2798 (1977).
(32) A. Padwa and N. Kamigata *J. Am. Chem. Soc.*, **99**, 1871 (1977).
(33) A. Padwa and P. H. J. Carlsen, *J. Am. Chem. Soc.*, **97**, 3682 (1975).
(34) More recently, Steglich and Fischer have found that the 1,1-cycloaddition of thermally generated nitrile ylides proceeds with retention of configuration; J. Fischer and W. Steglich, *Angew. Chem., Int. Ed. Engl.*, **18**, 167 (1979).
(35) D. Bethell, "Organic Reactive Intermediates", S. P. McManus, Ed., Academic Press, New York, 1973, p 101.
(36) G. B. Gill and M. R. Willis, "Pericyclic Reactions", Chapman and Hall, London, 1974, p 154.
(37) A. Steigel, J. Sauer, D. A. Kleier, and G. Binsch, *J. Am. Chem. Soc.*, **94**, 2770 (1972).
(38) L. Garanti and G. Zecchi, *J. Chem. Soc., Perkin Trans 1*, 116 (1980).
(39) L. Chiodini, L. Garanti, and G. Zecchi, *Synthesis*, 603 (1978).

5-methylene-4,5-dihydro-1*H*-1,2-benzodiazepine (**24**) occurs as a competitive or alternative reaction in those cases where $R_3 = CH_3$.[17]

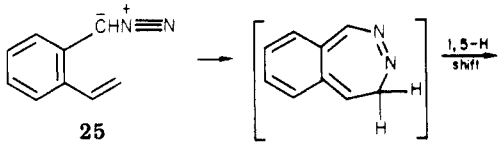


23 **20**

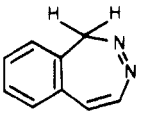


22 **24**

One additional point worth noting is that the cyclization of nitrilimine **7** to diazanorcaradiene **20** is closely related to the formation of benzoannelated 3*H*-1,2-diazepines via the 8π-electrocyclization reaction of unsaturated diazo compounds.[40-42] Sharp and co-workers have recently shown that diazo compounds with α,β-aromatic and γ,δ-olefinic unsaturation undergo 1,7-ring closure to give 2,3-benzodiazepines.[40-42] The mechanism suggested involves an initial electrocyclization of **25** to **26** followed by a 1,5-suprafacial sigmatropic hydrogen shift which gives **27** and restores the aromaticity of the aromatic ring.

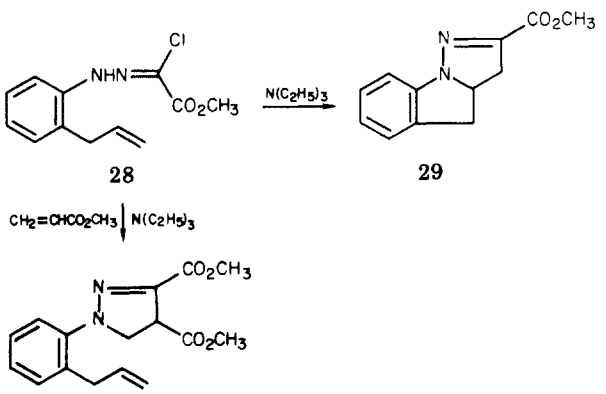


25 **26**



27

In view of the stringent spatial requirements associated with intramolecular dipolar cycloadditions,[9] we thought it worthwhile to consider what effect a variation in the spatial proximity between the nitrilimine and the π bond would have on the course of the reaction. To this end we synthesized methyl chloroglyoxylate (*o*-allylphenyl)-hydrazone (**28**). The only product obtained from treating **28** with triethylamine in benzene was methyl 9,9a-dihydro-1*H*-pyrazolo[2,3a]indole-2-carboxylate (**29**). This product was identified on the basis of its characteristic 100-MHz NMR spectrum ($CDCl_3$) which showed a set of doublet of doublets at δ 2.88 (1 H, J = 18.0, and 6.7 Hz), 2.92 (1 H, J = 10.0, 8.0 Hz), 3.09 (1 H, J = 10.0, 8.0 Hz), 3.24 (1 H, J = 18.0, 11.5 Hz), a singlet at δ 3.73 (3 H), a doublet of doublet of triplets at δ 4.55 (1 H, J = 11.5, 10.0, 6.7 Hz), and a multiplet at δ 6.8–7.3 (4 H). The intramolecular cyclization of **28** is a particularly interesting case in that it proceeds exclusively in the 1,3 sense. When the



28 **29**

30

reaction was carried out in the presence of methyl acrylate, the normal Δ^2-pyrazoline **30** was obtained as the exclusive product. With this system, the transition state for cycloaddition of the nitrilimine generated from chlorohydrazone **28** allows easy attainment of the "parallel-plane approach" of the dipole and olefin and, consequently, intramolecular 1,3-dipolar cycloaddition readily occurs. Clearly, the spatial relationship of the nitrilimine and dipolarophile p orbitals plays an extremely important role in controlling the mode of intramolecular cycloaddition.

In conclusion, the intramolecular dipolar cycloaddition of nitrilimines is a synthetically useful and mechanistic intriguing process. It is evident from our data that a distortion from the normal "parallel plane approach of addends" can have a major effect on the course of the cycloaddition process. The hybrid of carbenic and dipolar 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.

Experimental Section[43]

Preparation of Ethyl Chloroglyoxylate (*o*-Vinylphenyl)hydrazone (1). To a mixture of 4 mL of concentrated hydrochloric acid, 4 mL of water, and 16 mL of methanol at 0 °C was added 0.59 g of *o*-aminostyrene followed by the addition of 0.70 g of solid sodium nitrite in small portions. After being stirred for 15 min, the solution was neutralized by the slow addition of the solid sodium bicarbonate. A sample of 0.82 g of sodium acetate dissolved in 10 mL of water was then added, followed by 0.83 g of ethyl 2-chloroacetoacetate in 5 mL of methanol. After being stirred for 1 h at 0 °C, the solution was extracted with ether and the combined extracts were washed with a saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure left 1.51 g of a green oil. This material consisted mostly of ethyl 2-chloro-2-[(*o*-vinylphenyl)azo]acetoacetate as evidenced from its 100-MHz NMR spectrum ($CDCl_3$): δ 1.31 (t, 3 H, J = 7 Hz), 2.38 (s, 3 H), 4.31 (q, 2 H, J = 7 Hz), 5.39 (dd, 1 H, J = 11, 2 Hz), 5.79 (dd, 1 H, J = 18, 2 Hz), 7.1–7.7 (m, 4 H). The crude oil was passed through a column of neutral alumina with benzene to give 1.1 g (85%) of a yellow oil which slowly solidified on standing. Crystallization from hexane gave ethyl chloroglyoxylate (*o*-vinylphenyl)hydrazone (**1**) as a light yellow solid: mp 64–65 °C; IR (KBr) 3.03, 3.28, 5.81, 6.15, 6.24, 6.44, 6.65, 6.90, 7.34, 7.71, 8.13, 8.38, 8.57, 9.40, 10.08, 10.83, 11.58, 13.13, 13.36, 14.73 μm;

(40) A. A. Reid, J. T. Sharp, H. R. Sood, and P. B. Thorogood, *J. Chem. Soc., Perkin Trans 1*, 2543 (1973).
(41) J. T. Sharp, R. H. Findlay, and P. B. Thorogood, *J. Chem. Soc., Perkin Trans 1*, 102 (1975).
(42) K. L. M. Stanley, J. Dingwall, J. T. Sharp, and T. W. Naisby, *J. Chem. Soc., Perkin Trans 1*, 1433 (1979).

(43) All melting points are corrected and boiling points uncorrected. Elemental analyses were performed by the Atlantic Microanalytical Laboratory. The infrared absorption spectra were determined on a Perkin-Elmer Infracord spectrophotometer, Model 137. The ultraviolet absorption spectra were measured with a Cary recording spectrophotometer, using 1-cm matched cells. The nuclear resonance spectra were determined at 60 MHz with a Varian T-60 spectrometer, at 100 MHz with a Varian XL-100 spectrometer, and at 90 MHz with a Varian EM-390 spectrometer.

NMR ($CDCl_3$, 100 MHz) δ 1.38 (t, 3 H, J = 7 Hz), 4.33 (q, 2 H, J = 7 Hz), 5.43 (dd, 1 H, J = 11, 2 Hz), 5.61 (dd, 1 H, J = 18, 2 Hz), 6.73 (dd, 1 H, J = 18, 11 Hz), 6.7–7.6 (m, 4 H), 8.46 (br s, 1 H); UV (95% ethanol) 322, 252, 222 nm (ϵ 21 800, 11 200, and 15 500); mass spectrum, m/e 216, 189, 157, 143, 142, 130, 129 (base), 128, 127, 117, 102, 101, 90, 89, 77.

Anal. Calcd for $C_{12}H_{13}N_2O_2Cl$: C, 57.03; H, 5.19; N, 11.09. Found: C, 57.02; H, 5.20; N, 11.08.

Treatment of Ethyl Chloroglyoxylate (*o*-Vinylphenyl)-hydrazone (1) with Triethylamine. To a solution containing 253 mg of **1** in 10 mL of benzene was added 500 mg of triethylamine in 2 mL of benzene at 25 °C. After being stirred at room temperature for 10 h, the reaction mixture was diluted with 50 mL of distilled water and extracted with benzene. The organic layer was washed with a saturated aqueous solution of sodium chloride and was then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure left 250 mg (99%) of a light yellow solid whose structure was assigned as ethyl 4,5-dihydro-5-chloro-1H-1,2-benzodiazepine-3-carboxylate (**3**) on the basis of the following data: mp 114–115 °C; IR (KBr) 3.09, 3.58, 5.85, 6.27, 6.59, 6.76, 6.94, 7.03, 7.28, 7.35, 7.46, 7.70, 8.07, 8.25, 8.31, 8.53, 8.93, 9.19, 9.50, 9.73, 10.62, 11.61, 12.07, 13.22, 13.71 μm; NMR ($CDCl_3$, 100 MHz) δ 1.31 (t, 3 H, J = 7 Hz), 3.02 (dd, 1 H, J = 17, 2 Hz), 3.87 (dd, 1 H, J = 17, 6 Hz), 4.23 (q, 2 H, J = 7 Hz), 5.36 (dd, 1 H, J = 6, 2 Hz), 6.8–7.3 (m, 4 H), 10.1 (br s, 1 H); mass spectrum m/e 217, 216, 165, 163, 157, 144, 143, 142, 130, 129 (base), 128, 127, 117, 116, 92, 91, 90, 89, 86, 77, 53; UV (dioxane) 329, 305, 243 nm (ϵ 13 900, 12 000, 6620).

Anal. Calcd for $C_{12}H_{13}N_2O_2Cl$: C, 57.03; H, 5.18; N, 11.08. Found: C, 57.08; H, 5.22; N, 11.07.

Attempts to purify the above chloride by thick-layer chromatography resulted instead in the formation of ethyl 4,5-dihydro-5-hydroxy-1*H*-1,2-benzodiazepine-3-carboxylate (**4**): mp 160–161 °C; IR (KBr) 3.08, 5.86, 6.07, 6.24, 6.74, 7.22, 7.29, 7.50, 7.66, 7.78, 7.83, 8.13, 8.41, 8.57, 8.87, 9.10, 9.53, 9.80, 10.57, 10.92, 11.46, 12.47, 13.14, 13.40 μm; NMR ($CDCl_3$, 100 MHz) δ 1.35 (t, 3 H, J = 7 Hz), 3.01 (dd, 1 H, J = 15, 2 Hz), 3.42 (dd, 1 H, J = 15, 8 Hz), 4.33 (q, 2 H, J = 7 *Hz*), 5.1 (br s, 1H), 5.14 (dd, 1 H, J = 8, 2 Hz), 6.8–7.4 (m, 4 H), 8.1 (br s, 1 H); mass spectrum, m/e 217, 216 (base), 180, 179, 178, 165, 154, 153, 152, 129, 128, 117, 116, 115, 90; UV (95% ethanol) 324, 229 nm (ϵ 16 300, 7500).

Anal. Calcd for $C_{12}H_{14}N_2O_3$: C, 61.52; H, 6.02; N, 11.96. Found: C, 61.54; H, 6.06; N, 11.98.

Further support for the above structures was obtained by their conversion to ethyl 1*H*-1,2-benzodiazepine-3-carboxylate (**2**). Thus heating a sample containing 505 mg of **3** in 10 mL of benzene containing excess sodium hydride afforded 419 mg (97%) of benzodiazepine (**2**) after standard workup. Similarly, when a 126-mg sample of **4** in benzene was treated with a trace of *p*-toluene sulfonic acid and the mixture was heated at reflux for 5 min, 115 mg (99%) of benzodiazepine **2** was obtained. Ethyl 1*H*-1,2-benzodiazepine-3-carboxylate (**2**) is a blood red crystalline solid: mp 107–108 °C; IR (KBr) 3.06, 5.84, 6.32, 6.90, 7.25, 7.33, 7.81, 7.93, 8.29, 8.50, 8.84, 9.28, 9.90, 10.50, 11.00, 11.50, 11.85, 12.22, 13.90 μm; NMR ($CDCl_3$, 100 MHz) δ 1.29 (t, 3 H, J = 7 Hz), 4.23 (q, 2 H, J = 7 Hz), 6.2–7.1 (m, 7 H); mass spectrum, m/e 216 (M^+, base), 178, 171, 157, 144, 143, 142, 129, 128, 118, 117, 116, 115, 114, 90, 89; UV (95% ethanol) 262, 217 nm (ϵ 18 300, 17 000).

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.71; H, 5.59; N, 12.96.

Treatment of Ethyl Chloroglyoxylate (*o*-Vinylphenyl)-hydrazone (1) with Silver Carbonate. To a solution containing 253 mg of ethyl chloroglyoxylate (*o*-vinylphenyl)hydrazone (**1**) in 50 mL of dry benzene was added 2 mL of hexamethylphosphoramide (HMPA) and 552 mg of silver carbonate. After being stirred for 22 h at room temperature in the dark, the reaction mixture was filtered through Celite, washed with several portions of distilled water followed by a saturated solution of sodium chloride, and then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure left 239 mg of a brown oil. Passage of this oil with benzene through a short column of basic alumina afforded 198 mg (92% of a golden oil, whose structure was assigned as ethyl 1*H*-cyclopropa[*c*]cinnoline-1a-(7b*H*)-carboxylate (**5**) on the basis of the following spectral data: IR (neat), 3.37, 5.81, 6.22, 6.65, 6.77, 6.90, 7.17, 7.27, 7.67, 7.97, 8.10, 8.51, 8.65, 9.01, 9.39, 9.75, 10.35, 10.95, 11.59, 12.90, 12.98, 13.42, 14.72 μm; NMR ($CDCl_3$, 100 MHz) δ 0.11 (dd, 1 H, J = 7, 4 Hz), 1.38 (t, 3 H, J = 7 Hz), 2.75 (dd, 1 H, J = 9, 4 Hz), 3.11 (dd, 1 H, J = 9, 7 Hz), 4.38 (q, 2 H, J = 7 Hz), 7.3–7.6 (m, 3 H), 8.22 (dd, 1 H, J = 5, 3 Hz); mass spectrum, m/e 316 (base, M^+), 154, 144, 143, 129, 128, 117; UV (dioxane) 279, 245 nm (ϵ 6300, 5860).

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.48; H, 5.62; N, 12.73.

Further support for the structure of cinnoline **5** was obtained by its thermal conversion to benzodiazepine **2**. A solution containing 150 mg of **5** in 25 mL of benzene was heated at reflux for 4.5 h. Removal of the solvent under reduced pressure followed by silica gel chromatography afforded a 94% yield of benzodiazepine **2**.

Acid-Catalyzed Ring-Opening Reactions of Ethyl 1*H*-Cyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (5). To a solution containing 150 mg of ethyl 1*H*-cyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (**5**) dissolved in 45 mL of dry benzene was added 10 mL of methanol and a few crystals of *p*-toluenesulfonic acid hydrate. After the mixture was stirred for 18 h at room temperature, 30 mL of a saturated sodium bicarbonate solution was added. The organic layer was washed with a saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to afford 171 mg (97%) of a solid, which was recrystallized from hexane–benzene to give a white crystalline solid, mp 125–126 °C, whose structure was assigned as ethyl 4,5-dihydro-5-methoxy-1*H*-1,2-benzodiazepine-3-carboxylate (**9**) on the basis of the following spectral data: IR (KBr) 3.12, 3.55, 5.90, 6.32, 6.90, 7.35, 7.80, 8.10, 8.35, 9.25, 9.80, 10.62, 11.53, 12.10, 12.75, 13.35 μm; NMR ($CDCl_3$, 100 MHz) δ 1.34 (t, 3 H, J = 7 Hz), 2.78 (dd, 1 H, J = 15, 2 Hz), 3.29 (s, 3 H), 3.61 (dd, 1 H, J = 15, 7 Hz), 4.28 (q, 2 H, J = 7 Hz), 4.57 (dd, 1 H, J = 7, 2 Hz), 6.8–7.3 (m, 4 H), 8.7 (br s, 1 H); mass spectrum m/e 220, 219, 207, 206, 205 (base) 180, 155, 154, 135, 129, 128, 127, 105, 91, 77; UV (methanol) 323, 224 nm (ϵ 16 400, 8670).

Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.98; H, 6.51; N, 11.27.

A sample of the corresponding ethyl ether (**10**) was prepared in an analogous fashion with ethanol as the solvent: mp 121–122 °C; IR (KBr) 3.04, 3.11, 3.22, 3.40, 5.90, 6.10, 6.27, 6.30, 6.53, 6.77, 6.81, 6.97, 7.20, 7.30, 7.61, 7.81, 8.05, 8.20, 8.45, 8.60, 8.71, 9.12, 9.35, 9.70, 10.12, 10.59, 11.25, 12.12, 12.97, 13.20, 13.40, 14.0 μm; NMR ($CDCl_3$, 100 MHz) δ 1.17 (t, 3 H, J = 7 Hz), 1.34 (t, 3 H, J = 7 Hz), 2.91 (dd, 1 H, J = 15, J = 15, 2 Hz), 3.49 (m, 3 H), 4.30 (q, 2 H, J = 7 Hz), 4.69 (dd, 1 H, J = 7, 2 Hz), 6.7–7.3 (m, 4 H), 8.7 (br s, 1 H); mass spectrum, m/e 246 (base), 217, 216, 207,180, 179, 178, 165, 144, 143, 142, 141, 133, 129, 128, 117, 116, 115, 105, 95, 91, 89, 83, 81, 78, 77; UV (95% ethanol) 324, 228 nm (ϵ 17 300, 8490).

Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 64.13; H, 6.93; N, 10.66.

The corresponding acetate **11** was also prepared from cinnoline **5** by stirring a 150-mg sample in benzene with 1 mL of glacial acetic acid in the presence of a catalytic quantity of *p*-toluenesulfonic acid for 18 h at room temperature. Aqueous sodium bicarbonate removal of the unreacted glacial acetic acid, washing with a saturated sodium chloride solution, and drying over anhydrous magnesium sulfate, followed by removal of the solvent, gave 185 mg (96%) of a crystalline solid, mp 155–156 °C, whose structure was identified as ethyl 4,5-dihydro-5-acetoxy-1*H*-1,2-benzodiazepine-3-carboxylate (**11**) on the basis of the following spectral data: IR (KBr) 3.19, 5.78, 5.88, 6.30, 6.79, 7.20, 7.56, 7.78, 8.14, 8.31, 8.91, 9.16, 9.60, 9.80, 10.61, 12.25, 13.22 μm; NMR ($CDCl_3$, 100 MHz) δ 1.35 (t, 3 H, J = 7 Hz), 2.02 (s, 3 H), 2.85 (dd, 1 H, J = 16, 2 Hz), 3.26 (dd, 1 H, J = 16, 7 Hz), 4.33 (q, 2 H, J = 7 Hz), 6.22 (dd, 1 H, J = 7, 2 Hz), 6.8–7.4 (m, 4 H), 8.90 (br s, 1 H); mass spectrum, m/e 217, 216, 157, 154, 144, 143, 142, 130, 129, 128, 118 (base), 117, 116, 90, 89, 86; UV (95% ethanol) 326, 228 nm (ϵ 15 900, 8970).

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.84, H, 5.86; N, 10.13.

A sample of acetate **11** was also prepared directly from hydrazone **1** in the following manner. A stirred mixture of hydrazone **1** (650 mg), triethylammonium acetate (8 g), and potassium acetate

(2 g) in 50 mL of dry benzene was heated at reflux for 3 h. After standard aqueous workup and removal of the solvent under reduced pressure, 705 mg (99%) of acetate 11 was obtained.

Trapping of the Nitrilimine Derived from Ethyl Chloroglyoxylate (*o*-Vinylphenyl)hydrazone (1) with Methyl Acrylate. A solution containing 253 mg of 1, 2 mL of HMPA, and 552 mg of silver carbonate in 50 mL of methyl acrylate was stirred for 19 h at room temperature in the dark. The solution was washed with water, extracted with ether, and dried over magnesium sulfate. Removal of the solvent under reduced pressure left 220 mg of an oil which was chromatographed on a thick-layer plate, a 1:1 ether–pentane mixture as the eluant. The major component present in the mixture was identified as benzodiazepine **2** (55%). The second component isolated from the thick-layer plate (38%) was a clear oil whose structure was assigned as dipolar cycloadduct 8 on the basis of its charactistic spectral data: IR (neat) 3.37, 5.76, 5.89, 6.15, 6.27, 6.41, 6.78, 6.91, 7.09, 7.27, 7.41, 7.60, 7.97, 8.29, 8.63, 9.02, 9.77, 10.90, 11.23, 12.03, 13.04 μm; NMR ($CDCl_3$, 100 MHz) δ 1.35 (t, 3 H, J = 7 Hz), 3.48 (m, 2 H), 3.54 (s, 3 H), 4.34 (q, 2 H, J = 7 Hz), 4.96 (dd, 1 H, J = 10, 10 Hz), 5.34 (dd, 1 H, J = 11, 1.5 Hz), 5.69 (dd, 1 H, J = 18, 1.5 Hz), 6.98 (dd, 1 H, J = 18, 11 Hz), 7.2–7.6 (m, 4 H); mass spectrum, m/e 302 (M^+), 243, 229, 199, 197 (base), 188, 171, 169, 144, 130, 117, 103, 77; UV (95% ethanol) 323, 238 nm (ε 13 800, 11 800).

Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.54; H, 6.03; N, 9.23.

Preparation of *cis*- and *trans*-β-Methyl-*o*-aminostyrene. To a flame-dried flask containing 7.3 g of magnesium turnings was added 32.7 g of ethyl bromide in 300 mL of anhydrous tetrahydrofuran at a rate to maintain a gentle reflux. After the addition was completed, the dark solution was heated at reflux for an additional 30 min. This solution was then added dropwise to a stirred solution of 16.3 g of *o*-formylacetanilide in 300 mL of anhydrous tetrahydrofuran at −78 °C. After the addition was complete, the mixture was allowed to warm to room temperature over a 3-h period and was then quenched by the addition of a dilute aqueous solution of hydrochloric acid. The mixture was extracted with benzene, the combined organic layers were washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure to leave behind 18.3 g (95%) of a viscous yellow oil. This crude oil was directly hydrolyzed and dehydrated by refluxing in a 3 N solution of hydrochloric acid in 200 mL of a 1:1 dioxane/water mixture for 1 h. The reaction mixture was then poured into 700 mL of ice–water and neutralized with solid sodium bicarbonate. After extraction with a solution of benzene, hexane, and methylene chloride, the combined extracts were washed with saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the dark residue was chromatographed on a silica gel column, using benzene as the eluant, to give *trans*-β-methyl-*o*-aminostyrene in 74% yield: bp 63–65 °C (0.6 mm); IR (neat) 2.96, 3.03, 3.15, 3.35, 3.48, 3.54, 6.20, 6.39, 6.75, 6.95, 7.30, 7.70, 7.82, 7.95, 8.67, 8.80, 9.63, 10.35, 11.68, 12.47, 13.36 μm; NMR ($CDCl_3$, 100 MHz) δ 1.89 (d, 3 H, J = 7 Hz), 3.64 (br s, 2 H), 5.9–7.3 (m, 6 H).

A solution containing 0.50 g of *trans*-β-methyl-*o*-aminostyrene in 500 mL of anhydrous benzene was irradiated for 45 min with a 550-W Hanovia lamp equipped with a Pyrex filter sleeve. After removal of the solvent under reduced pressure, the crude photolysate was passed through a short silica gel column with a 1:1 benzene–hexane mixture to give 0.48 g (96%) of a light yellow oil. The NMR analysis of this oil revealed it to be a 2:1 mixture of the cis and trans isomers. *cis*-β-Methyl-*o*-aminostyrene showed the following NMR ($CDCl_3$, 100 MHz) spectrum: δ 1.69 (dd, 3 H, J = 7, 2 Hz), 3.6 (br s, 2 H), 5.6–7.2 (m, 6 H).

Preparation of Methyl Chloroglyoxylate (*o*-β-Methylstyryl)hydrazone. To a mixture consisting of 25 mL of concentrated hydrochloric acid, 25 mL of distilled water, and 50 mL of methanol at 0 °C was added 1.69 g of a 2:1 mixture of *cis*- and *trans*-β-methyl-*o*-aminostyrene. The mixture was diazotized by the dropwise addition of 2.97 g of isoamyl nitrite in 15 mL of methanol. After 15 min, the solution was neutralized with solid sodium bicarbonate, followed by the addition of 2.5 g of potassium acetate and 2.10 g of methyl 2-chloroacetoacetate. After warming to room temperature over a 2-h period, the reaction mixture was diluted with enough distilled water to dissolve the precipitated salts and was then extracted with a solution of benzene, hexane, and methylene chloride. The organic extracts were combined and dried over anhydrous magnesium sulfate. After concentration under reduced pressure, the residue was passed through a column of neutral alumina with benzene, affording a mixture of the cis (12) and trans (13) isomers of methyl chloroglyoxylate (*o*-β-methylstyryl)hydrazone in the same isomer ratio as the initial mixture of *cis*- and *trans*-aminostyrenes. This mixture was separated into its component parts via medium-pressure silica gel chromatography, using a 1:1 benzene/hexane mixture as the eluant. The pure cis isomer (12) was the first component eluted from the column (1.44 g, 67%): mp 31–32 °C; IR (neat) 3.03, 3.33, 5.75, 6.46, 6.66, 6.91, 6.99, 7.60, 7.80, 8.13, 8.45, 9.33, 10.71, 12.72, 13.23, 14.00 μm; NMR ($CDCl_3$, 100 MHz) δ 1.67 (dd, 3 H, J = 7, 2 Hz), 3.89 (s, 3 H), 6.02 (dq, 1 H, J = 11, 7 Hz), 6.38 (d, 1 H, J = 11 Hz), 6.9–7.3 (m, 3 H), 7.58 (d, 1 H, J = 8 Hz), 8.5 (br s, 1 H); UV (95% ethanol) 327 nm (ε 23 450); mass spectrum, m/e 252 (M^+), 217, 216, 184, 158, 156, 155, 143, 142, 132, 131 (base), 130, 129, 128, 117, 115.

Anal. Calcd for $C_{12}H_{13}N_2O_2Cl$: C, 57.03; H, 5.19; N, 11.09. Found: C, 56.97; H, 5.24; N, 11.07.

The second component eluted from the column contained the trans isomer (13): mp 49–50 °C; IR (KBr) 3.04, 3.42, 5.81, 6.50, 6.70, 7.00, 7.28, 7.79, 8.15, 8.37, 8.59, 9.40, 10.38, 11.60, 12.75, 13.30 μm; NMR ($CDCl_3$, 100 MHz) δ 1.96 (d, 3 H, J = 6 Hz), 3.95 (s, 3 H), 6.18 (dq, 1 H, J = 16, 6 Hz), 6.51 (d, 1 H, J = 16 Hz), 6.9–7.7 (m, 4 H), 8.64 (br s, 1 H); UV (95% ethanol) 325, 248, 223 nm (ε 20 270, 12 380, 16 220); mass spectrum m/e 252 (M^+), 217, 216, 184, 158, 157, 156, 1558 143, 142, 132,131 (base), 130, 129, 128, 117, 115.

Anal. Calcd for $C_{12}H_{13}N_2O_2Cl$: C, 57.03; H, 5.19; N, 11.09. Found: C, 56.98; H, 5.20; N, 11.07.

Treatment of Methyl Chloroglyoxylate (*o*-*trans*-β-Methylstyryl)hydrazone (13) with Silver Carbonate. A 500-mg sample of hydrazone 13 in 50 mL of a 5% solution of hexamethylphosphoramide (HMPA) in anhydrous benzene at room temperature was treated with 1.10 g of silver carbonate in the dark for 24 h. At the end of this time, the solution was filtered through Celite, washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give 411 mg (95%) of a golden oil. The NMR spectrum of this oil indicated it to contain only methyl 1*H*-*exo*-methylcyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (15): NMR ($CDCl_3$, 100 MHz) δ 0.55 (dq, 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), 7.3–7.6 (m, 3 H), 8.1–8.3 (m, 1 H). When this material was allowed to stir for an additional 24 h, the exo isomer was partially converted into the corresponding endo isomer. Heating a sample of the pure exo isomer at 80 °C in benzene for 2 h gave rise to a 3:1 mixture of the *endo*- (14) and *exo*-cyclopropa[*c*]cinnolines (15). The pure endo isomer (14) could be obtained from this mixture by fractional crystallization from hexane and was a gold solid: mp 98–99 °C; IR (KBr) 2.90, 3.39, 5.82, 6.20, 6.63, 6.93, 7.21, 7.73, 8.00, 8.32, 8.53, 8.71, 8.96, 9.35, 9.79, 10.75, 11.07, 12.50, 12.66, 12.50, 12.66, 12.77, 13.02, 13.51, 14.58 μm; NMR ($CDCl_3$, 100 MHz) δ 0.33 (d, 3 H, J= 6.5 Hz), 2.94 (dq, 1 H, J = 9, 6.5 Hz), 3.30 (d, 1 H, J = 9 Hz), 3.95 (s, 3 H), 7.3–7.6 (m, 3 H), 8.1–8.3 (m, 1 H); UV (dioxane) 283 nm (ε 6030); mass spectrum, m/e 216 (M^+), 184, 158, 157, 156, 155, 143, 142, 131 (base), 130, 129, 125.

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.49; H, 5.67; N, 12.89.

All attempts to obtain a pure sample of the endo isomer failed since it was readily converted into a 3:1 equilibrium mixture of *endo*- and *exo*-cyclopropa[*a*]cinnolines.

A solution containing 250 mg of (*cis*-β-methylstyryl)hydrazone 12 was allowed to react for 3 h at 25 °C in the dark in 50 mL of a 5% HMPA solution in benzene with 2 equiv of silver carbonate. After normal workup the NMR spectrum showed only the presence of the *endo*-cyclopropa[*a*]cinnoline 14. Heating the endo isomer produced a 3:1 equilibrium mixture of 14 and 15. The same equilibrium mixture was also obtained by stirring the endo isomer in benzene at room temperature for 48 h.

Thermolysis of Methyl 1*H*-*endo*-Methylcyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (14). A 40-mg sample of pure

endo-cyclopropa[*a*]cinnoline (**14**) was dissolved in 0.5 mL of benzene-d_6 and sealed under vacuum in a heavy-walled NMR tube. The solution was heated at 80 °C and the course of the thermolysis monitored by NMR spectroscopy. After the solution was heated for 1 h, the typical equilibrium mixture of 3:1 *endo*- (**14**) to *exo*- (**15**) cyclopropa[*a*]cinnolines was obtained. Further heating slowly transformed the mixture of isomers into a new compound, which was identified as methyl 1*H*-4-methyl-1,2-benzodiazepine-3-carboxylate (**17**) by its spectral characteristics, with a half-life of 20 h. After being heated for 90 h, the tube was opened and after removal of the solvent, the residue was crystallized from hexane to give 35 mg (88%) of analytically pure methyl 1*H*-4-methyl-1,2-benzodiazepine-3-carboxylate (**17**): mp 87–88 °C; IR (KBr) 3.09, 5.80, 6.24, 6.61, 6.83, 6.95, 7.22, 7.33, 7.68, 7.88, 8.21, 8.37, 8.55, 8.85, 9.15, 9.45, 9.61, 9.85, 10.20,11.46, 12.27, 12.64, 12.82, 13.17, 13.35, 14.43 μm; NMR ($CDCl_3$, 100 MHz) δ 2.00 (d, 3 H, J = 2 Hz), 3.77 (s, 3 H), 6.5–7.4 (m, 6 H); UV (95% ethanol) 322, 228 nm (ε 18 180, 8230); mass spectrum, m/e 216 (base, M^+), 201, 185, 184, 158, 157, 156, 155, 142, 129, 128.

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; H, 12.96. Found: C, 66.70; H, 5.63; h, 12.90.

Reaction of Methyl 1*H*-*endo*-Methylcyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (14) with Acetic Acid. A solution containing 216 mg of *endo*-cyclopropa[*a*]cinnoline **14** in 50 mL of benzene containing 0.5 mL of glacial acetic acid was heated at reflux for 2 h. The cooled solution was washed with a saturated aqueous solution of sodium bicarbonate and sodium chloride, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give 275 mg (100%) of a lightly colored solid. Digestion of this material for 1 h in 25 mL of a refluxing 1:1 solution of acetone/hexane afforded methyl *cis*-4,5-dihydro-5-acetoxy-4-methyl-1*H*-1,2-benzodiazepine-3-carboxylate (**18**) as a white microcrystalline solid of analytical purity: mp 199–200 °C; IR (KBr) 3.11, 5.82, 6.30, 6.78, 7.00, 7.31, 7.60, 7.81, 8.35, 8.86, 9.12, 9.78, 10.08, 10.51, 10.94, 11.29, 11.54, 11.91, 12.40, 13.01, 13.30 μm; NMR ($CDCl_3$, 100 MHz) δ 0.88 (d, 3 H, J = 8 Hz), 1.95 (s, 3 H), 3.88 (s, 3 H), 4.00 (dq, 1 H, J = 8, 7 Hz), 5.97 (d, 1 H, J = 7 Hz), 6.9–7.5 (m, 4 H), 9.2 (br s, 1 H); ^{13}C NMR (20 MHz, Me_2SO-d_6) 16.89, 20.79, 37.17, 51.75, 77.31, 117.79, 123.01, 129.34, 132.71, 133.90, 142.58, 165.90, 169.27 ppm; UV (95% ethanol) 322, 228 nm (ε 18 180, 8230); mass spectrum, m/e 276 (M^+), 217, 216, 184, 158, 157, 156, 155, 143, 142, 141, 131 (base), 130, 129, 128, 115, 89.

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.87; H, 5.87; N, 10.11.

Treatment of *cis*-dihydrobenzazepine **18** with a trace of *p*-toluenesulfonic acid resulted in epimerization to give the corresponding trans isomer **19** as a white crystalline solid: mp 150–151 °C; IR (KBr) 3.07, 5.90, 6.29, 6.82, 6.96, 7.28, 7.40, 7.60, 8.09, 8.43, 8.51, 9.11, 9.25, 10.36, 11.15, 12.20, 12.50, 12.91, 13.23 μm; NMR ($CDCl_3$, 100 MHz) δ 1.25 (d, 3 H, J = 7 Hz), 2.38 (s, 3 H), 3.78 (s, 3 H), 4.27 (d, 1 H, J = 4 Hz), 4.62 (m, 1 H), 6.8–7.4 (m, 3 H), 7.68 (d, 1 H, J = 8 Hz), 8.9 (br s, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) 17.02, 21.61, 40.61, 52.34, 79.19, 114.71, 124.80, 127.85, 128.54, 129.83, 134.28, 144.57, 164.58 ppm; UV (95% ethanol) 337, 226 nm (ε 7800, 13 170); mass spectrum, m/e 276 (M^+), 219, 218, 217, 216, 203, 201, 189, 188, 186, 158, 157, 156, 155, 143, 142, 131, 130 (base), 129, 115, 103, 102, 101, 91.

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; N, 5.84; N, 10.14. Found: C, 60.91; H, 5.92; N, 10.10.

Preparation of Methyl Chloroglyoxylate (*o*-Allylphenyl)hydrazone (28). A solution containing 4.00 g of *o*-allylaniline dissolved in a mixture consisting of 25 mL of concentrated hydrochloric acid, 25 mL of distilled water, and 50 mL of methanol was diazotized at 0 °C by the dropwise addition of 6.0 g of isoamyl nitrite. After 15 min, the solution was neutralized by the slow addition of powdered sodium bicarbonate. This was followed by the addition of 6.0 g of potassium acetate and 4.7 g of methyl 2-chloroacetoacetate. The solution was allowed to warm to room temperature over 2 h and was then extracted with methylene chloride and hexane. The combined organic extracts were washed with a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was then passed through a column of neutral alumina with benzene to give methyl chloroglyoxylate (*o*-allylphenyl)hydrazone (**28**) in 78% yield: mp 47–48 °C; IR (neat) 3.09, 3.45, 5.78, 6.30, 6.45, 6.64, 6.86, 6.99, 7.58, 7.75, 8.06, 8.40, 8.55, 9.35, 10.02, 10.71, 12.73, 13.35 μm; NMR ($CDCl_3$, 100 MHz) δ 3.34 (d 2 H, J = 6 Hz), 3.81 (s, 3 H), 5.12 (m, 2 H), 5.80 (m, 1 H), 6.7–7.5 (m, 4 H), 8.4 (br s, 1 H); UV (95% ethanol) 323, 232 nm (ε 17 280, 7430).

Anal. Calcd for $C_{12}H_{13}N_2O_2Cl$: C, 57.03; H, 5.19; N, 11.09. Found: C, 57.05; H, 5.20; N, 11.08.

Base Treatment of Methyl Chloroglyoxylate (*o*-Allylphenyl)hydrazone (28). To a solution of 504 mg of hydrazone **28** in 50 mL of anhydrous benzene at 80 °C was added 0.5 mL of triethylamine. After being heated for 24 h, the cooled solution was sequentially washed with a dilute aqueous solution of hydrochloric acid and a saturated aqueous solution of sodium chloride. After the solution was dried over anhydrous magnesium sulfate the solvent was removed under reduced pressure to give 430 mg (100%) of a light yellow solid, mp 136–137 °C, which was identified as methyl 9,9a-dihydro-1*H*-pyrazolo[2,3a]indole-2-carboxylate (**29**) on the basis of the following spectral data: IR (KBr) 3.45, 5.80, 6.35, 6.80, 6.98, 7.28, 7.42, 7.49, 7.71, 8.05, 8.35, 8.52, 8.84, 9.02, 9.70, 12.11, 12.58 12.85, 13.43, 14.50 μm; NMR ($CDCl_3$, 100 MHz) δ 2.88 (dd, 1 H, J = 18.0, 6.7 Hz), 2.92 (dd, 1 H, J = 10.0, 8.0 Hz), 3.09 (dd, 1 H, J = 10.0, 8.0 Hz), 3.24 (dd, 1 H, J = 18.0, 11.5 Hz), 3.73 (s, 3 H), 4.55 (ddt, 1 H, J = 11.5, 10.0, 6.7 Hz), 6.8–7.3 (m, 4 H); UV (95% ethanol) 322, 237 nm (ε 4230, 2160); mass spectrum, m/e 216 (M^+, base), 215, 157, 156, 130, 129, 117, 116, 100, 91, 90, 89, 59.

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.56; H, 5.59; N, 12.96. Found: C, 66.57; H, 5.64; N, 12.94.

When the base-induced reaction of **28** was carried out in the presence of a 10 mol excess of methyl acrylate a 98% yield of dimethyl 1-(*o*-allylphenyl)-2-pyrazoline-3,4-dicarboxylate (**30**) was obtained as a pale yellow oil: IR (neat) 3.45, 5.75, 5.82, 6.14, 6.25, 6.45, 6.73, 6.96, 7.95, 9.05, 9.75, 10.80, 11.30, 12.65, 13.10 μm; NMR ($CDCl_3$, 100 MHz) δ 3.3–3.7 (m, 4 H), 3.60 (s, 3 H), 3.87 (s, 3 H), 4.9–5.3 (m, 3 H), 5.9–6.3 (m, 1 H), 7.20 (s, 4 H); UV (95% ethanol) 324, 240 nm (ε 12 330, 2670); mass spectrum, m/e 302 (M^+), 243, 212, 211 (base), 210, 183, 143, 131, 130, 115, 91, 59.

Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.70; H, 6.07; N, 9.20.

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Registry No. **1**, 65480-24-2; **2**, 65480-37-7; **3**, 76466-66-5; **4**, 74066-49-2; **5**, 71987-88-7; **8**, 71987-89-8; **9**, 76466-67-6; **10**, 76466-68-7; **11**, 74066-56-1; **12**, 71987-90-1; **13**, 71987-91-2; **14**, 72028-86-5; **15**, 71987-92-3; **17**, 71987-93-4; **18**, 76466-69-8; **19**, 76466-70-1; **28**, 76479-89-5; **29**, 76466-71-2; **30**, 76466-72-3; *o*-aminostyrene, 3867-18-3; ethyl 2-chloroacetoacetate, 609-15-4; ethyl 2-chloro-2-[(*o*-vinylphenyl)azo]acetoacetate, 76466-73-4; ethyl bromide, 74-96-4; *o*-formylacetanilide, 13493-47-5; *o*-(1-hydroxypropyl)acetanilide, 76466-74-5; *trans*-β-methyl-*o*-aminostyrene, 33149-71-2; *cis*-β-methyl-*o*-aminostyrene, 33149-72-3; methyl 2-chloroacetoacetate, 4755-81-1; *o*-allylaniline, 32704-22-6.