Solids were removed by filtration, and evaporation of the MnO_2-free ether gave a dark oil which solidified on cooling. Recrystallization from ether/*n*-hexane gave long yellow needles of **6**: 0.6 g; mp 62–63 °C. **6** was identical (IR, mixture melting point) with that prepared from the hydrolysis of **5**. Other methods of oxidation (CrO_3–CH_3COOH, $KMnO_4$–acetone) were inferior to the above method.

Hydrolysis of Mesoionic Compound 8 to *O*-Benzoylmandelanilide (9). Mesoionic **8** (100 mg) was suspended in 20 mL of ether. Dilute HCl (10 mL) was added, and the mixture was stirred at room temperature until the orange color of **8** disappeared (20 min). The dried ether layer was evaporated and the residue was recrystallized from methanol to give 40 mg of **9**: mp 181–182 °C (lit.[15] mp 177 °C); IR 3225, 1725, 1665, 1600, 1550, 1500, 1280, 1260, 1250, 1115, 750, 710 cm^{-1}; NMR δ 6.4 (s, 1 H), 7.3 (m, 13 H), 8.1 (m, 3 H). Compound **9** was also prepared by the heating of mandelanilide (**7**, 0.5 g) and benzoyl chloride (0.5 g) in pyridine (5 mL) for 5 h on a steam bath. Dilution with water gave a white solid which was recrystallized from methanol: 0.65 g; mp 182–183 °C. The IR, NMR, and mixture melting point were identical with those of **9** isolated from the hydrolysis of **8**.

Preparation of 5 from 6. Phenylglyoxanilide (**6**, 0.6 g) was dissolved in 970 mL of dry ether. Sodium wire (0.5 g) was added, and the mixture was stirred at room temperature for 10 min after which a solution of 0.4 g of benzoyl chloride in 30 mL of dry ether was added dropwise. The mixture was stirred for an additional 20 min. The mixture was filtered and evaporated to leave a dark yellow residue which was treated with methanol (5 mL). The resulting white solid was collected by suction filtration, washed with methanol, and dried to give 0.26 g of **5**, mp 131 °C. The product was identical (IR and mixture melting point) mmp) with **5** prepared by the photolytic or thermal rearrangement of **1**.

Exo and Endo Adducts 10a and 10b. Mesoionic **8** (0.3 g) was mixed with toluene (100 mL) at room temperature. *N*-Phenylmaleimide (0.18 g) was added to the mixture. The orange-red color of **8** disappeared immediately. Evaporation of toluene followed by separation of the major two products by thick-layer chromatography ($CHCl_3$/$PhCH_3$, 1:1) gave 60 mg of *exo*-**10a** [mp 240–242 °C; IR 1735, 1712, 1600, 1500, 1375, 1330, 1195, 1180, 1025, 1010, 760, 750, 695, 640 cm^{-1}; NMR δ 4.05 (d, 1, J = 4 Hz), 4.46 (d, 1, J = 4 Hz), 7.1, 7.4, 8.1 (m, 20)] and 130 mg of *endo*-**10b**: mp 253–254 °C; IR 1735 (sh), 1716, 1600, 1500, 1375, 1335, 1195, 1090, 1010, 930, 870, 815, 750, 718, 690 cm^{-1}; NMR δ 3.91 (1 H, J = 4 Hz), 4.30 (1 H, J = 4 Hz), 6.8, 7.2, 7.4, 7.6, 7.8 (m, 20 H). Anal. Calcd for $C_{31}H_{22}N_2O_4$: C, 76.52; H, 4.55; N, 5.76. Found for **10a**: C, 76.07; H, 4.57; N, 5.53. Found for **10b**: C, 76.19; H, 4.71; N, 5.72. Heating of either **10a** or **10b** above their melting points resulted in the formation of a red product which is presumed to be **8**.

Registry No. **1**, 30121-36-9; **5**, 80263-47-4; **6**, 4732-66-5; **7**, 4410-33-7; **8**, 80263-48-5; **9**, 24334-54-1; *exo*-**10a**, 80263-49-6; *endo*-**10b**, 80300-25-0; *N*-phenylmaleimide, 941-69-5.

(15) Passerini, M. *Gazz. Chim. Ital.* **1921**, *51*, 181–189.

Synthesis and Intramolecular Cycloaddition Reactions of Some 3-Substituted 6-Azidohexa-2,4-dienoate Esters

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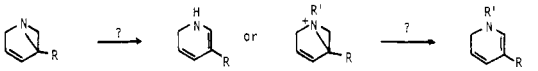
Several 3-substituted (methyl, *n*-butyl, phenyl) 6-azidohexa-2,4-dienoate esters were synthesized by conjugate addition of [(*Z*)-3-[(tetrahydropyranyl)oxy]-1-propenyl]copper to the appropriate acetylenic ester, followed by conversion to the azide by depyranylation, mesylation, and azide substitution. In the methyl and butyl cases, the addition was nonstereoselective under the conditions used, while the phenyl case gave nearly completely the product of anti addition. The azides all undergo intramolecular cycloaddition to form 3a,6-dihydro-3*H*-pyrrolo[1,2-*c*][1,2,3]triazoles at rates which depend upon the stereochemistry and substitution of the 6-azidohexa-2,4-dienoate. All of these adducts are unstable with respect to decomposition to a 2-substituted pyrrole, again at rates which are both substituent and solvent dependent. Under certain circumstances, the 3a,6-dihydro-3*H*-pyrrolo[1,2-*c*][1,2,3]triazoles are converted to the open chain valence tautomers which are α-diazo-2,5-dihydropyrrole-2-acetate esters. Possible factors contributing to the observed substituent and stereochemical effects are considered.

1,2-Dihydropyridines are useful synthetic intermediates, but there exist limitations on the types of substitution patterns which are routinely available.[1] One significant but elusive structure is the 5-substituted-1,2-dihydro system.[2] We wished to explore the possibility that 1-azabicyclo[3.1.0]hex-3-enes or the corresponding salts might be thermally converted to 1,2-dihydropyridines. We



decided to approach the desired bicyclic system via an intramolecular cycloaddition, following a pattern observed for substituted 5-azido-1-pentenes by Logothetis.[3] This paper describes the synthesis of the required azides and the observation that the intramolecular cycloadducts are unstable with respect to decomposition to 2-substituted pyrroles and/or α-diazo-2,5-dihydropyrrole-2-acetate esters. Both the rates of formation and subsequent decomposition of the intramolecular cycloadducts are sensitive

(1) 1-Alkyl-1,2-dihydropyridines: P. Beeken, J. N. Bonfiglio, I. Hasan, J. J. Piwinski, B. Weinstein, K. A. Zollo, and F. W. Fowler, *J. Am. Chem. Soc.*, *101*, 6677 (1979). 1-(Acyloxy)-1,2-dihydropyridines: F. W. Fowler, *J. Org. Chem.*, **37**, 1321 (1972). 2-Substituted-1-acyl-1,2-dihydropyridines: C. S. Giam, E. E. Knaus, and F. M. Pasutto, *J. Org. Chem.*, **39**, 3565 (1974); R. E. Lyle, J. L. Marshall, and D. L. Comins, *Tetrahedron Lett.*, 1015 (1977). 1,4-Dihydropyridines with 3- or 3,5-substitution by electronegative groups: U. Eisner and J. Kuthan, *Chem. Rev.*, 1 (1972).

(2) A recent approach by C. Marazano, M.-T. LeGoff, J.-L. Fourey, and B. P. Das, *Chem. Commun.*, 389 (1981), appears promising. Nucleophilic adducts capable of serving as synthetic equivalents have also been studied: D. S. Grierson, M. Harris, and M.-P. Husson, *J. Am. Chem. Soc.*, *102*, 1064 (1980).

(3) A. L. Logothetis, *J. Am. Chem. Soc.*, **87**, 749 (1965).

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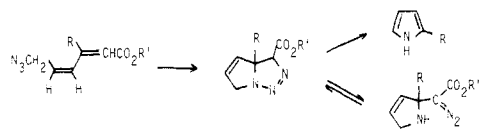
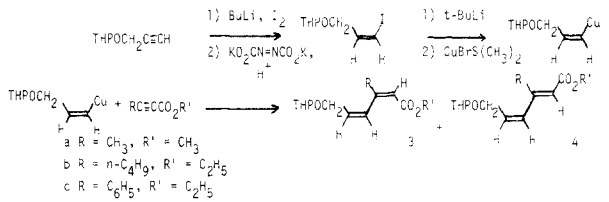
to the substitution and stereochemistry of the 6-azido-2,4-hexadienoate esters. In the course of these studies, some new facets of the chemistry of 7*H*-oxepin-2-ones, the lactones of 6-hydroxyhexa-2,4-dienoic acids, were also revealed.

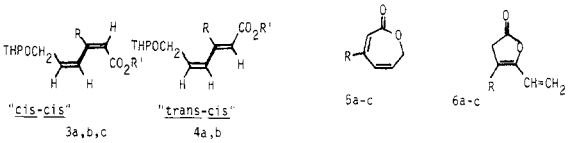


Results

We chose, as the initial system for investigation, esters of 3-substituted-6-azidohexa-2,4-dienoic acids. It appeared these compounds could be made satisfactorily and with good flexibility as to the identity of the 3-substituent, by addition of a protected (3-hydroxy-*cis*-1-propenyl)copper to 3-substituted propynoate esters. Conversion of propargyl alcohol to the THP-protected (*Z*)-vinyl iodide **2** proceeded via closely precedented[4] iodination and diimide reduction of 2-tetrahydropyranyl propargyl ether. The vinyl iodide was converted to a vinylcopper reagent, taking advantage of the useful summary of Helquist[5] concerning various conditions for formation of vinylcopper intermediates. Since high stereoselectivity was not essential to our purposes and the addition was quite sluggish at −78 °C, the addition reactions were conducted at −20 °C. Under these conditions methyl 2-butynoate and ethyl 2-heptynoate both gave a mixture of *Z* and *E* isomers **3a**, **3b** and **4a**, **4b** which were separable by chromatography. Under similar conditions, ethyl phenylpropynoate gave a single major adduct **3c**. The stereochemistry of the products under these conditions is presumably determined by the equilibrium composition of the anionic adduct.[6]

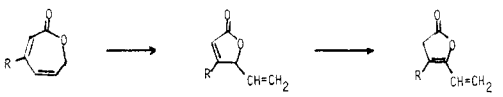


The stereochemistry of these adducts were ascertained by a combination of chemical and NMR data. The THP group could be removed from the adducts by treatment with *p*-toluenesulfonic acid at 60 °C for 10 min. Under these conditions **3a**, **3b**, and **3c**, but not **4a** or **4b**, gave rise to byproducts formulated as the 3-substituted 7*H*-oxepin-2-ones **5a–c**, the lactones formed by cyclization of the deprotected alcohols. Lactonization could be completed by stirring the product mixture with *p*-toluenesulfonic acid in chloroform for 1 h at room temperature. Since lactonization requires that both double bonds be "cis", the series **3a–c** was assigned the "cis-cis" geometry, whereas **4a** and **4b** were assigned "trans-cis" stereochemistry.[7] Because



of the mode of preparation[6] and *J* values of 12 Hz for the vinyl protons on C-4 and C-5 for all of the adducts, the cis configuration at C-4–C-5 appears firm. Each of the substances **5** showed the loss of the ester alkoxy group, the absence of a hydroxyl group, and the mass of molecular ion is in agreement with lactonization having occurred. The carbonyl absorption was near 1700 cm^{-1}. The NMR spectrum of **5a**, which is typical of the series, shows the methyl group at 1.96 ppm (d, J = 0.9 Hz) and the methylene group at 4.41 ppm (d, J = 6 Hz). The C-3 proton of the oxepinone ring is a narrow multiplet with incompletely resolved small (J < 2 Hz) coupling at 6.16 ppm. The remaining vinyl protons are mutually coupled, J = 10 Hz, and appear as a multiplet whose shape is reproduced by the additional J values $J_{3,5}$ = 1.8 Hz and $J_{6,7}$ = 6.0 Hz. The δ values are 6.26 for H-5 and 6.33 for H-6. These features of the NMR spectrum are consistent with the 7*H*-oxepin-2-one structure and rule out possible tautomers.

The oxepinones **5a–c** proved to be thermally unstable, partially isomerizing on distillation (bath temperature ~ 120 °C) or completely on refluxing in benzene for 2 h to 5-vinyl-3*H*-furan-2-ones **6a–c**. The furanones show a shift of the carbonyl group to 1750 cm^{-1}, and the NMR spectra are definitively in support of the assignment of the 3*H*-furan-2-one structure. In particular for **6a** the C-2 methylene group appears as a sharp singlet at 2.97 ppm, and the vinyl protons appear as a pattern typical of a terminal vinyl group. Previous workers have reported partial or complete isomerization of 5-phenyl[8] and 5-vinyl[9,10] 5*H*-furanones to the corresponding 3*H*-furanones. Thus a possible path for the observed isomerization could be via the 5*H* tautomer.



There was no indication (NMR monitoring) of accumulation of the 5*H*-furanone intermediate, nor of an equilibrium concentration of this tautomer at the completion of the isomerization. The ring contraction can be formulated as a dioxa-Cope-type rearrangement (eq 1). A similar transition state for a rearrangement in the opposite direction has been proposed by Rhodes and Watson (eq 2).[11] Although there have been scattered report of 7*H*-oxepin-2-ones in connection with the study of photochemical behavior of 3*H*-oxepin-2-ones, there does not appear to have been prior study of the thermal stability of these compounds.[12] Acid-catalyzed conversion of 7-phenyl-7*H*-oxepin-2-one to 5-styryl-3*H*-furan-2-one occurs, but by a process which is formulated as an ionic reaction.[10,13]

(4) A. F. Kluge, K. G. Untch, and J. H. Fried, *J. Am. Chem. Soc.*, **94**, 9256 (1972).

(5) A. Marfat, P. R. McGuirk, and P. Helquist, *J. Org. Chem.*, **44**, 3888 (1979).

(6) Prior workers have found the lithium–iodine exchange reaction to be stereospecific with retention of configuration: G. Cahiez, D. Bernard, and J. F. Normant, *Synthesis*, 245 (1976). The addition step is a stereoselective syn addition at −40 to −75 °C, but stereoequilibration occurs at higher temperatures: J. B. Siddall, M. Biskup, and J. H. Fried, *J. Am. Chem. Soc.*, **91**, 1853 (1969); R. J. Anderson, V. L. Corbin, G. Cotterrell, G. R. Cox, C. A. Hendrick, F. Schaub, and J. B. Siddall, *ibid.*, **97**, 1197 (1975). Vinylcopper reagents retain configuration even under the condition where the stereoselectivity of the addition step is lost: F. Naf and P. Degen, *Helv. Chim. Acta*, **54**, 1939 (1971).

(7) The descriptions *E,Z* and cis,trans both change for stereochemically analogous compounds within the series. For convenience, we use "cis,trans" as it refers to the hexadienoate chain.

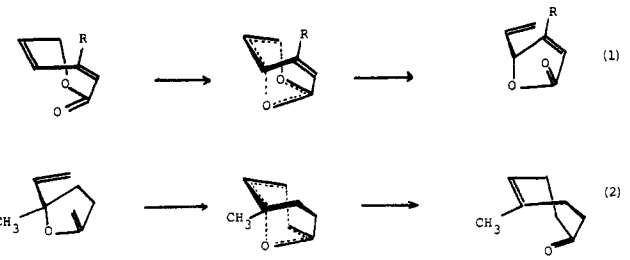
(8) J. L. Herrmann, M. H. Berger, and R. H. Schlessinger, *J. Am. Chem. Soc.*, **101**, 1544 (1979); D. Caine and A. S. Frobese, *Tetrahedron Lett.*, 5167 (1978); K. Iwai, H. Kosugi, H. Uda, and M. Kawai, *Bull. Chem. Soc. Jpn.*, **50**, 242 (1977).

(9) F. W. Machado-Araujo and J. Gore, *Tetrahedron Lett.*, **22**, 1969 (1981).

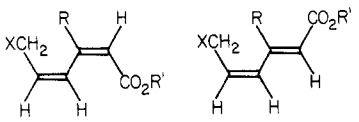
(10) N. Hoshi, H. Hagiwara, and H. Uda, *Chem. Lett.*, 1295 (1979).

(11) S. J. Rhoads and J. M. Watson, *J. Am. Chem. Soc.*, **93**, 5813 (1971).

(12) A. Kawamoto, H. Kosugi, and H. Uda, *Chem. Lett.*, 807 (1972).



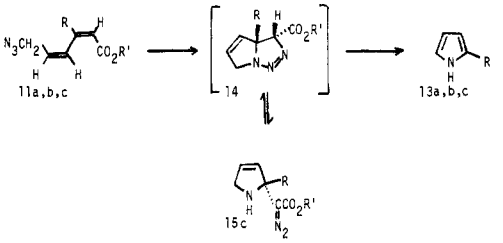
Despite the tendency for lactonization, it was possible to prepare mesylates from alcohols **7a–c** by reaction with methanesulfonyl chloride immediately after removal of the THP group. The mesylates of the "trans-cis" alcohols **8a** and **8b** were prepared without complication. Each of the mesylates was then subjected to reaction with sodium azide in dimethylformamide at room temperature. The results obtained revealed a very sensitive dependence of the course of the reaction on both the geometry of the C-2–C-3 double bond and the steric bulk of the 3-substituent. The following paragraphs summarize the behavior of the azides **11a–c** and **12a–b**.



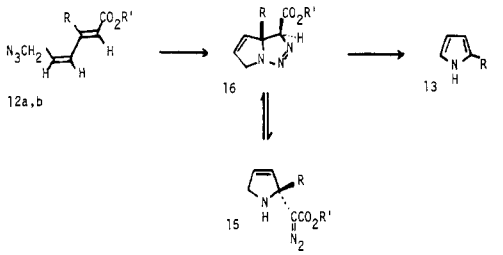
"cis-cis" 7, 9, 11 "trans-cis" 8, 10, 12

7, X = OH
8, X = OH
9, X = OSO_2CH_3
10, X = OSO_2CH_3
11, X = N_3
12, X = N_3

Reaction of mesylate **9a** with sodium azide in DMF at room temperature for 16–20 h gave 2-methylpyrrole, **13a**, as the principal product. The behavior of **9b** was completely similar, 2-butylpyrrole being formed in high yield under the conditions of azide preparation. Azide **11c**, the phenyl derivative, was slightly more stable and an azide (47% yield) contaminated by 2-phenylpyrrole (17% yield) could be obtained and adequately characterized by NMR and infrared data. At 80 °C (6 h) the azide was cleanly converted to 2-phenylpyrrole (**13c**). At a somewhat lower temperature (~55 °C, 1.5 h optimum) a rather unstable isomer of the azide, formulated as ethyl α-diazo-2-phenyl-2,5-dihydropyrrole-2-acetate. **15c**, was obtained. At a higher temperature (80 °C) this compound gave 2-phenylpyrrole. The evidence for the structure is as follows: diazo band at 2090 cm^{-1}, exchangeable proton (NH) at δ 2.1, and IR NH stretch at 3350 cm^{-1}, signals 6.12 (m, 2 H) and 3.82 ppm (d, $J < 2$ Hz, 2 H) assignable to the protons of the ring system. Hoye and Deerfield[14] have observed reversible formation of α-diazopiperidine-2-acetates after intramolecular cycloadditions of a homologous 7-azidohept-2-enoate system, which lacks the C-4–C-5 unsaturation in the present system. Huisgen and Szeimes observed that triethylamine caused an analogous ring opening in a monocyclic system, methyl 1-phenyl-1,2,3-triazoline-4-carboxylate.[15] From these observations on the "cis-cis" series, we infer that intramolecular cycloadditions of **11a** and **11b** are faster than for **11c** and that the adducts, structures **14a–c**, are all unstable under the conditions of formation. The observation of **15c** and its subsequent conversion of 2-phenylpyrrole provides circumstantial evidence for the formation of the adducts.

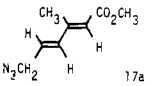


Attention was then turned to the "trans-cis" series and preparation of azides **12a** and **12b** proceeded normally and the azides had expected spectroscopic properties. Azide **12a** gave rise to minimal, if any, pyrrole when heated at 80 °C in benzene for 6 h. The main product at this point was the very sensitive intramolecular adduct **16a**. The



NMR spectrum (360 MHz) of the adduct shows the vinyl protons as multiplets at 5.73 and 5.82 ppm which are coupled to the nonequivalent protons of the ring methylene group. The methylene group appears as an AB system at 4.72 and 4.08 ppm (J = 16 Hz), also showing the fine coupling to the vinyl protons. The methyl group is at 1.31 ppm and the C-3 ring proton appears at 5.14 ppm as a singlet. On standing (0 °C, 6 days) or attempted chromatography, the adduct **16a** was converted to the α-diazo ester **15a**, which was similar in spectral properties to the diazo ester **15c** isolated in the phenyl series. In the infrared, the NH stretch appeared at 3360 cm^{-1} and there was a strong diazo band at 2090 cm^{-1}. The proton NMR spectrum (360 MHz) shows the vinyl protons as a multiplet centered at 5.90 ppm. The methylene group appears as an AB pattern centered at 3.77 ppm, both doublets having additional fine coupling. The CCH_3 group is at 1.55 ppm.

It is possible to follow the formation and decomposition of **16a** by NMR. The conversion of **12a** to **16a** was ~30% complete after 1 h at 78 °C in $CDCl_3$, while formation of 2-methylpyrrole was about 25% complete after 4 h. Half-lives of 2 h for **12a** and ~6–8 h for **16a** in $CDCl_3$ are indicated by these results. At 110 °C in benzene-d_6 the disappearance of **16a** was nearly complete after 3 h. In both of these experiments a peak at 4.73 ppm, attributed to methyl diazoacetate, grew proportionately with the formation of the pyrrole. In addition, peaks attributable to a new azide **17a**, the "trans-trans" isomer, developed and accounted for about 30% of the startng material. This azide, which is sterically incapable of intramolecular cycloaddition, was stable at 110 °C over the course of the reaction (3 h). The extent of formation of the "trans-trans" azide was unaffected by the presence of a weak nucleophile, pyridine, in the reaction mixture.



(13) N. Hoshi, H. Hagiwara, and H. Uda, *Chem. Lett.*, 1291 (1979).
(14) T. R. Hoye and D. W. Deerfield, Abstract 127, Division of Organic Chemistry, 181 National Meeting of the American Chemical Society, Atlanta, GA, March 29–31, 1981.
(15) Unpublished results of G. Szeimes, quoted by R. Huisgen, R. Grashey, and J. Sauer, "Chemistry of Alkenes", S. Patai, Ed., Wiley, New York, 1964, p 839.

When **16a** was stirred with sodium azide in DMF at room temperature under the conditions of azide formation, it was cleanly converted to 2-methylpyrrole. This result indicates that the differing behavior between the "cis-cis" and "trans-cis" series is the result of a significant rate difference for the *formation* of the intramolecular cycloadduct.

With the butyl analogue **10b**, conversion to 2-butylpyrrole occurred in good yield in benzene at ~70 °C (1.5 h). By monitoring the reaction by NMR in $CDCl_3$, we observed peaks characteristic of an intermediate adduct (**16b**) to maximize at approximately 40 min at 78 °C, with the reaction eventually going cleanly to the pyrrole and ethyl diazoacetate (δ 4.74). Thus, relative to **12a**, the formation of pyrrole is somewhat accelerated in the "trans-cis" series by the introduction of the butyl substituent, with rough estimate being $t_{1/2}$ = 0.7 h and $t_{1/2}$ = 1 h for **12b** and **16b**, respectively, at 78 °C.

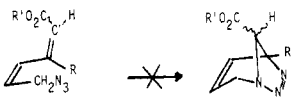
Complete NMR data for the synthetic intermediates **3**, **4**, **7–11**, and **12** are given in Table I as supplementary material.

Discussion

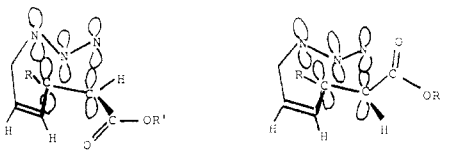
The following questions are posed by these results.

1. Why do the "cis-cis" azides cyclize at (or below) room temperature while the "trans-cis" isomers require heating?
2. What is the nature of the pyrrole-forming reaction from the cycloadduct?
3. Why is the methyl-substituted "trans-cis" azide **12a** more reluctant to form a pyrrole than the butyl analogue **12b**?
4. How does the isomerization of "trans-cis" azide **12a** to the "trans-trans" isomer **17a** occur?

The first question is one of relative reactivity and concerns substitutent effects on cycloaddition reactions, a subject for which good theoretical guidance exists.[16] First, as far as can be detected, an alternative cycloaddition mode which might be possible is avoided by all the azides. The



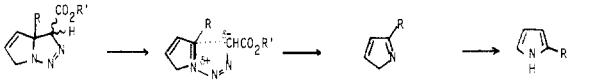
regioselectivity which is observed is in accord with that commonly found and predicted for cycloadditions of azides to electron-deficient dipolarophiles.[17] Turning to the operative cycloaddition, the transition states for the "cis-cis" and "trans-cis" families are pictured. Estimates



of $t_{1/2} \leq 4$ h at 25 °C for **11a** and $t_{1/2} \geq 60$ h at 25 °C for **12a** were extracted from the preparative studies. There must be a difference between the two isomers of at least a factor of 15 in the rate of intramolecular cycloaddition. Inspection of models shows that the products of the "cis-cis" series avoid an eclipsing of the C-3 substituent and the ester group. This may, in part, account for the greater facility of the "cis-cis" isomers for cycloaddition. This factor, however, cannot be the only one operating, since it would suggest that **12a**, where the eclipsing interaction involves a methyl group, should be more reactive toward addition than **12b**, which carries the larger butyl group. The opposite is the case. A second significant difference in the "cis-cis" and "trans-cis" transition states is the possibility of secondary orbital interactions with the carbonyl group. These appear more feasible in the "cis-cis" transition state, where the carbomethoxy group is "endo" than in the "trans-cis" where it is "exo". We propose as the answer to the first question posed above, then, primarily secondary orbital interactions between the azido and the carbonyl groups with perhaps some contribution from a simple steric effect.

The postulated stabilizing factor is equivalent to the interactions which give rise to the "Alder rule", the preference for endo addition, in Diels–Alder reactions. The existence of such effects would be stereochemically unobservable in intermolecular cycloadditions of azides to dipolarophiles. Even with stereoisomeric dipolarophiles, any stereochemical preferences in the direction of approach of the azide would be obscured by the planar (or rapidly inverting) nature of the triazoline product.

The observation that adduct **16a** has a half-life of 6–8 h at 80 °C in benzene but is converted to 2-methylpyrrole at room temperature in DMF under the conditions of the azide-forming reaction establishes two important points. The facile transformation of the cis-cis azides to pyrroles under the conditions of their formation and the contrasting stability of the trans-cis azides to the same conditions is the result of the substantial difference in the rate of formation of the cycloadduct. Secondly, the pyrrole-forming reaction is quite solvent dependent, being more rapid in DMF than benzene. We propose that pyrrole formation occurs via a polar process which is similar in character to a reverse Mannich reaction.



The comparative reactivity between **12a** and **12b** and **16a** and **16b** are estimated as ~3:1 and ~8:1, respectively, the butyl compound being the more reactive in each case. These differences are presumably steric in origin. An increased ground-state repulsion in **12b** due to the increased bulk of both the alkyl and ester group could increase the reactivity of **12b** by raising the ground-state energy, relative to **12a**. In the elimination step, the same increased steric repulsion would be expected to favor the retrocycloaddition.

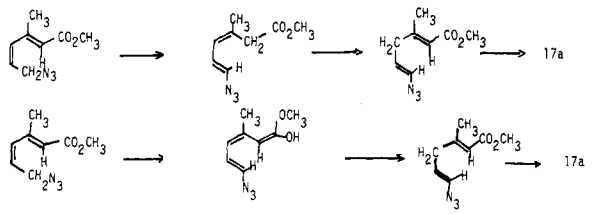
The phenyl system cannot be meaningfully discussed with regard to any stereochemical effects on intramolecular cycloaddition in the absence of stereoisomer **12c**. The data do show that the effect of the phenyl group in **11c**, relative to the alkyl substituents in **11a** and **11b**, is to somewhat retard the intramolecular cycloaddition.

The final point raised by the results is the mechanism for isomerization of the trans-cis azide **12a** to the trans-trans azide **17a**, a reaction which takes place at 80–110 °C in competition with intramolecular cycloaddition. We had originally thought that the most likely explanation might be a reversible conjugate addition by an adventitious nucleophile, but added pyridine had no apparent effect. It therefore seems more likely that a strictly thermal isomerization process is competing with intramolecular cycloaddition. We have been unable to locate any published reports of thermal geometric isomerizations of (*E*,*Z*)-hexadienoate (trans-cis sorbate) esters, but at least two mechanisms, a 1,5-hydrogen shift or an enolization via a 1,7-hydrogen shift could lead to the observed C-4–C-5

(16) K. N. Houk, *Top. Curr. Chem.*, **79**, 1 (1979); K. Fukui, *ibid.*, **15**, 1 (1970); K. N. Houk in "Pericyclic Reactions", A. P. Marchand and R. E. Lehr, Ed., Academic Press, New York, 1977, Vol. 2, pp 181–272.

(17) K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc.*, **95**, 7301 (1973).

isomerization. Barring large specific substituent effects, the former seems unlikely to occur at the observed temperature.[18] The latter process, while without direct precedent, appears a possibility. Further study of the cis-trans isomerization at the C-4–C-5 double bond would be required before a definitive conclusion can be made about this process.



Experimental Section

2-[(3-Iodoprop-2-ynyl)oxy]tetrahydropyran (1). The tetrahydropyranyl ether of propargyl alcohol[19] (15 g, 0.11 mol) was dissolved in ether (150 mL) and the solution cooled to −78 °C. There was then added 0.12 mol of *n*-butyllithium as a 2.3 M solution in hexane. The resulting suspension was stirred at −78 °C for 0.5 h and then iodine (30 g) dissolved in ether (150 mL) was slowly added. The solution was allowed to come to room temperature, with a small additiona. amount of iodine being added if necessary to maintain a slight excess of iodine (brown color). After 15 min at room temperature, the solution was washed with sodium thiosulfate solution, sodium bicarbonate, and saturated sodium chloride. The ether was dried and evaporated and the residue distilled to give 2-(3-iodoprop-2-ynoxy)tetrahydropyran: 25.9 g, 90%, bp 90 °C (0.1 mm).

2-[(*Z*)-(3-Iodoprop-2-enyl)oxy]tetrahydropyran (2). A mixture of the iodoacetylene 1 (15.7 g, 59 mmol) and dipotassium azodicarboxylate (15.1 g, 77 mmol) in methanol (40 mL) was stirred at 0 °C. To this mixture was added slowly a methanolic solution of acetic acid (154 mmol of acetic acid diluted with an equal volume of methanol). The addition was completed in about 30 min and the solution was then stirred 2 h at room temperature. At this point the product was about 80% the desired vinyl iodide, with the remainder being unreacted starting material and saturated iodide. Spinning-band distillation gave 2 (11.1 g, 70%), free of starting material but contaminated by 5–10% of the saturated iodide.

***Z,Z* and *E,Z* Isomers of Methyl 3-Methyl-6-[(tetrahydropyranyl)oxy]hexa-2,4-dienoate (3a and 4a).** A solution of 2 (2.0 g, 7.5 mmol) in ether (30 mL) was cooled to −78 °C. With stirring there was slowly added *tert*-butyllithium (15.0 mmol) as a 1.2 M solution in pentane. A precipitate formed during addition and the mixture was stirred for 1 h after addition was complete. A solution of *pure* cuprous bromide–dimethyl sulfide complex[20] (7.5 mmol) in dimethyl sulfide (15 mL) was slowly added by syringe. This resulted in a yellow-brown solution, which was brought to −45 °C (CH_3CN–CO_2 bath) and stirred for 2 h. To this solution was added methyl 2-butynoate (7.5 mmol) in ether (3 mL). After the addition, the solution stirred for 4 h at −25 °C before methanol (3 mL) was added. The solution was allowed to warm to room temperature and then hydrolyzed with saturated ammonium chloride solution and the product extracted into ether. Evaporation of this ether left an oil and some inorganic material. The mixture was shaken with ether and filtered. The ether layer was washed with ammonium chloride solution, sodium bicarbonate solution, and saturated sodium chloride before being dried and evaporated. The isomers were separated by chromatography on silica gel 60 (Merck). With 10% ether in hexane eluent, the *Z,Z* isomer **3a** (18%) was eluted after the *E,Z* isomer **4a** (26%). Analytical samples were obtained by Kugelrohr distillation. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found **3a**: C, 64.98; H, 8.40. Found **4a**: C, 65.05; H, 8.41.

***Z,Z* and *E,Z* Isomers of Ethyl 3-Butyl-6-[(tetrahydropyranyl)oxy]hexa-2,4-dienoate (3b and 4b).** A procedure analogous to that for **3a** and **4a** gave **3b** and **4b** in 26% and 44% yield, respectively, after separation by chromatography. The *Z* isomer **3b** was contaminated by a small amount of material derived from the saturated iodide contaminant, possibly 1,6-bis[(tetrahydropyranyl)oxy]hexane, which was identical in chromatographic polarity and only partially removed by distillation. Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found for **4b**: C, 68.71; H, 9.53.

Ethyl (*E,Z*)-3-Phenyl-6-[(tetrahydropyranyl)oxy]hexa-2,4-dienoate (3c). The procedure was analogous to those above except that the reaction time at −25 °C was 6 h. The yield of **3c** after chromatographic purification was 56% with only ~2% of the *Z* isomer being indicated by NMR. This material was not distillable at 0.1 mm and was used directly for the preparation of **7c**.

3-Methyl-7*H*-oxepin-2-one (5a), 4-Methyl-5-vinyl-3*H*-furan-2-one (6a), and Methyl (*Z,Z*)-6-Hydroxy-3-methylhexa-2,4-dienoate (7a). A mixture of **3a** (1.5 mmol) and *p*-toluenesulfonic acid (5 mg) in methanol (5 mL) was stirred at room temperature for about 1 h at which point TLC indicated complete solvolysis and partial lactonization. The two components were difficult to separate chromatographically. The optimum conditions for isolation of the alcohol **7a** (46% yield) involved extracting the mixture into ether, washing with sodium bicarbonate, heating to benzene for 2 h, which converted **5a** to **6a**, and separation by chromatography on silica gel 60, using 20% ether in hexane as eluent. The preparation of **5a** was optimized by warming the original acid solution to 60 °C for 1 h. **5a**: NMR ($CDCl_3$, 360 MHz) δ 6.25–6.35 (m, 2 H), 6.16 (s, 1 H), 4.41, (d, 2 H), 1.96, (s, 3 H). **5a** could be completely converted to **6a** by refluxing in benzene for 2 h. Only **6a** could be distilled unchanged: NMR ($CDCl_3$) δ 6.47 (d, 1 H), 5.8, (m, 2 H), 2.97 (s, 2 H), 1.97 (s, 3 H). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found for **6a**: C, 67.49; H, 6.53.

Methyl (*E,Z*)-6-Hydroxy-3-methylhexa-2,4-dienoate (8a). A solution of **4a** (1 mmol) and *p*-toluenesulfonic acid (5 mg) was heated to 60 °C for 5 min in methanol (5 mL). The reaction mixture was poured into saturated bicarbonate and the product extracted with ether. After drying and evaporation, the residue was pure **8a** (98% yield). The analytical sample was prepared by Kugelrohr distillation. NMR data are given in Table I (supplementary material). Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.29; H, 7.77.

Ethyl (*Z,Z*)-3-Butyl-6-hydroxyhexa-2,4-dienoate (7b), 3-Butyl-7*H*-oxepin-2-one (5b), and 4-Butyl-5-vinyl-3*H*-furan-2-one (6b). Procedures as described above gave **7b** in 70% yield. Formation of **5b**: NMR ($CDCl_3$) δ 6.33 (s, 2 H), 6.16 (s, 1 H), 4.39 (d, 2 H), 2.23 (t, 2 H), 1.2–1.7 (m, 2 H), 0.85 (t, 3 H). **6b**: NMR ($CDCl_3$) δ 6.51 (d, 1 H), 5.8 (m, 2 H), 3.02 (s, 2 H), 2.28 (t, 2 H), 1.1–1.7 (m, 4 H), 0.9 (t, 3 H), also occurred under similar conditions. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found for **6b**: C, 72.20; H, 8.51.

Ethyl (*E,Z*)-3-Butyl-6-hydroxyhexa-2,4-dienoate (8b). The alcohol was obtained in 72% yield as described for **8a**. NMR data are given in Table I.

Ethyl (*E,Z*)-6-Hydroxy-3-phenylhexa-2,4-dienoate (7c), 3-Phenyl-7*H*-oxepin-2-one (5c), and 4-Phenyl-5-vinyl-3*H*-furan-2-one (6c). The hydrolysis was carried out by heating **3c** in ethanol with *p*-toluenesulfonic acid for 10 min at 78 °C. The alcohol **7c** (60% yield) was purified by chromatography and distilled using a Kugelrohr apparatus. Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.29; H, 7.77.

Fractions containing a mixture of **5c** and **6c** were heated to give pure **6c**, which was distilled using a Kugelrohr apparatus: NMR ($CDCl_3$) δ 7.34 (m, 5 H), 6.58 (d, 1 H), 6.39 (d, 1 H), 5.92 (t, 1 H), 3.42 (s, 2 H). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found for **6c**: C, 67.49; H, 6.53.

Standard Conditions for Mesylation and Azide Synthesis (9a–c, 10a,b). A standard set of conditions for azide synthesis was used for all of the alcohols. The product mixtures were then processed according to the individual circumstances described in the sections below. In all cases the mesylate intermediates were examined by NMR and found to be >95% pure. A solution of the alcohol (0.50 mmol) in methylene chloride (5 mL) was cooled

(18) C. W. Spangler, *Chem. Rev.*, **76**, 187 (1976).
(19) H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, *J. Chem. Soc.*, 3646 (1950).
(20) H. O. House, C.-Y. Chu, J. M. Wilkins, and M. J. Umen, *J. Org. Chem.*, *40*, 1460 (1975).

to −5 °C and treated with 0.75 mmol of triethylamine, followed by slow addition of methanesulfonyl chloride (0.60 mmol) in methylene chloride (1 mL). After being stirred for 30 min at −5 °C, the mixture, which contained precipitated triethylamine hydrochloride, was poured into cold 5% hydrochloric acid. The methylene chloride layer was separated and washed successively with 5% hydrochloric acid and sodium bicarbonate solution and was then dried over potassium carbonate, before being evaporated to give the mesylates as fluid oils. (Yields were 87–99% based on weights at this point.)

The mesylate was then dissolved in dry dimethylformamide (4 mL) and powdered sodium azide (0.75 mmol) was added to the solution. The mixture was then stirred at room temperature for 16–20 h. The solution was poured into water and the product was extracted with ether. The ether layer was washed with sodium bicarbonate solution and sodium chloride solution before being dried and rapidly evaporated at less than 45 °C on a rotary evaporator. Product characterizations are discussed for the individual azides.

Formation of 2-Methylpyrrole (13a) during Preparation of Azide 11a. The dominant product from the procedure for preparation of **11a** was 2-methylpyrrole, as identified by the characteristic NMR peaks at 5.9, 6.1, and 6.3 ppm. No azide was detectable at the end of the standard reaction period and only 2-methylpyrrole was isolated (48% yield) after preparative layer chromatography. The identification of the pyrrole was further confirmed by its infrared and mass spectra.

Formation of 2-Butylpyrrole (13b) during Preparation of Azide 11b. As for **11a**, 2-butylpyrrole was obtained as the only product from the attempted synthesis of **11b**. Isolation by preparative layer chromatography gave nearly a quantitative yield of **13b** identified by its NMR, IR, and mass spectra.

Preparation of Azide 11c Accompanied by 2-Phenylpyrrole (13c). After subjecting **7c** to the standard mesylation and azide formation conditions, two principal materials were evident from TLC and the NMR spectrum of the mixture. Comparison with pure samples permitted assignment of peaks and estimate of yields for 2-phenylpyrrole (**13c**; 17%) and the azide **11c** (47%). The pure pyrrole was isolated by preparative TLC: mp 130 °C (lit.[21] mp 131–132 °C).

Methyl (*E,Z*)-6-Azido-3-methylhexa-2,4-dienoate (12a). The product starting from alcohol **10a** was essentially pure azide **12a** in 85% yield. NMR data are given in Table I.

Ethyl (*E,Z*)-6-Azido-3-butylhexa-2,4-dienoate (12b). The product starting from alcohol **10b** was essentially pure azide **12b** in 89% yield. NMR data are given in Table I.

Conversion of Ethyl (*E,Z*)-6-Azido-3-phenylhexa-2,4-dienoate (11c) to α-Diazo Ester (15c). A solution of azide **11c** (108 mg, 0.42 mmol) in benzene (3 mL) was warmed to about 55 °C for 1.5 h. The mixture was then partially resolved by chromatography on a silica TLC plate, using 1:1:3 ether/ethyl acetate/hexane for development. The partially overlapping bands were eluted from the silica with chloroform containing 0.5% triethylamine. After a second similar separation, the isolated yield of **15c** was 27 mg (25%), the remainder of the material being 2-phenylpyrrole. NMR for **15c**: δ 7.29 (m, 5 H), 6.1 (m, 2 H), 4.08 (q, 2 H), 3.82 (d, J = 1 Hz, 2 H), 2.08 (s, 1 H), 1.12 (t, 3 H).

Conversion of 11c to 2-Phenylpyrrole.[22] When the azide was heated to refluxing benzene for 2.5 h (130 mg in 15 mL of benzene), 2-phenylpyrrole was isolated in 50% yield and recrystallized from chloroform–petroleum ether to give pure 2-phenylpyrrole: mp 130 °C. A small amount (~10%) of a substance whose NMR spectrum is consistent with it being an azide with a C-4–C-5 trans double bond was also obtained.

When the azide **11c** was stirred with 1% acetic acid in ether for 36 h at room temperature, the pyrrole was formed in ~80% yield.

Conversion of 12a to Triazoline 16a, Diazo Ester 15a, and Azide 17a.[22] A solution of azide **12a** (43 mg) was refluxed in benzene for 3.5 h and then the solvent carefully removed on the rotary evaporation to give 43 mg of material shown by NMR to consist of traizoline **16a** (70%) and the 4,5-trans azide **17a** (30%). NMR for **16a**: δ 5.7–5.8 (m, 2 H), 4.72, 4.08 (ABd, J = 16 Hz, 2 H), 5.14 (s, 1 H), 3.78 (s, 3 H), 1.31 (s, 3 H). A similar experiment was carried out in a sealed NMR tube with benzene-d_6 containing ~2% pyridine. The product mixture as analyzed by NMR was the following: triazoline, 45%; diazo ester, 25%; and trans azide, 30%. Attempted separation of the mixture on silica led to complete conversion of **16a** to **15a**. NMR for **15a**: δ 5.8–5.9 (m, 2 H), 3.77 (m, 2 H), 3.71 (s, 3 H), 1.9 (s, 1 H), 1.55 (s, 3 H).

Conversion of 12a to 2-Methylpyrrole and Azide 17a.[22] A solution of **12a** (16 mg) in benzene-d_6 (0.5 mL) was placed in an NMR tube and heated to 110 °C. After 3 h at 110 °C there was recovered 15 mg of product shown by NMR to consist of 2-methylpyrrole (70%) and "trans-trans" azide **17a** (30%). NMR for **17a** ($CDCl_3$): δ 6.37 (d, J = 16 Hz, 1 H), 6.03, (dt, J = 16, 6 Hz, 1 H), 5.84 (s, 1 H), 3.91 (d, J = 6 Hz, 2 H), 3.69 (s, 3 H), 2.29 (s, 3 H).

Conversion of 16a to 2-Methylpyrrole and Azide 17a.[22] A solution of **16a** (18 mg) in benzene-d_6 (0.5 mL) was heated at 110 °C for 3 h as above. After workup 12 mg of material consisting of the same **13a–17a** mixture was obtained.

Acknowledgment. The high-field (360 MHz) NMR spectra were recorded on instrumentation provided by a major equipment grant to the Chemistry Department by the National Science Foundation, NSF Grant CH E80-07925.

Registry No. **1**, 80293-84-1; **2**, 80288-03-5; **3a**, 80288-04-6; **3b**, 80288-05-7; **3c**, 80288-06-8; **4a**, 80288-07-9; **4b**, 80288-08-0; **5a**, 80288-09-1; **5b**, 80288-10-4; **5c**, 80288-11-5; **6a**, 80288-12-6; **6b**, 80288-13-7; **6c**, 80288-14-8; **7a**, 80288-15-9; **7b**, 80288-16-0; **7c**, 80288-17-1; **8a**, 80288-18-2; **8b**, 80288-19-3; **9a**, 80288-20-6; **9b**, 80288-21-7; **9c**, 80288-22-8; **10a**, 80288-23-9; **10b**, 80288-24-0; **11a**, 80288-25-1; **11b**, 80288-26-2; **11c**, 80288-27-3; **12a**, 80288-28-4; **12b**, 80288-29-5; **13a**, 636-41-9; **13b**, 1551-10-6; **13c**, 3042-22-6; **15a**, 80288-30-8; **15c**, 80288-31-9; **16a**, 80288-32-0; **17a**, 80288-33-1; methyl 2-butynoate, 23326-27-4; ethyl 2-heptynoate, 16930-95-3; ethyl 3-phenyl-2-propynoate, 2216-94-6.

Supplementary Material Available: A table showing chemical shift data for NMR spectra measured at 90 MHz is given for the acyclic synthetic intermediates having structures **3**, **4**, **7–11**, and **12** (1 page). Ordering information is given on any current masthead page.

(21) G. Wittig and B. Reichel, *Chem. Ber.*, **96**, 2851 (1963).

(22) In view of the potential for explosion of the alkyl diazoacetates generated in these reactions, due precautions should be taken; N. E. Searle, "Organic Syntheses", Collect. Vol. 4, Wiley, New York, 1963, p 424.