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STRUCTURE OF TETRAHYDROPYRIDAZINES FORMED FROM 1-ISOPROPYL-3,4-DIMETHYL-1,2-DIAZA-1,3-BUTADIENE AND METHYL VINYL KETONE

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In contrast to the cis isomer, trans-1-isopropyl-3,4-dimethyl-1,2-diaza-1,3-butadiene reacts with methyl vinyl ketone to give a mixture of cis and trans isomers of 5- and 6-acetyl-1-isopropyl-3,4-dimethyl-Δ^2-tetrahydropyridazines. The preponderance of the cis isomer in the case of 5-substituted tetrahydropyridazines constitutes evidence for the existence of secondary orbital interactions of the acetyl group of the dienophile with the C=C bond of the diene component.

The observance of the endo principle [1] for a nucleophilic diene component containing a C=C−N=N fragment [2] has not been investigated. For its verification it was necessary to examine the reaction of olefins with terminally substituted 1,2-diaza-1,3-butadienes.

We have found that α,β-unsaturated azo compounds of this type [3] actually react with methyl acrylate, methyl vinyl ketone, and acrylonitrile to give four-component mixtures of 1,4-cycloaddition products (mixtures of structural isomers and stereoisomers). Their similar physicochemical characteristics made it impossible for us to isolate them in pure form or to reliably identify the Δ^2-tetrahydropyridazines formed, except for the products of the reaction of methyl vinyl ketone with 1-isopropyl-3,4-dimethyl-1,2-diaza-1,3-butadiene (I).

This azadiene exists in the form of Z,E and E,E isomers [3, 4], of which the Z,E isomer, which was isolated in pure form, was found to be inactive in the diene synthesis because of the steric hindrance that arises during its conversion to the s-cis conformation necessary for the reaction. On the other hand, the pure E,E isomer, as expected, readily forms cycloaddition products with methyl vinyl ketone by undergoing the reaction in the cisoid conformation. A mixture of tetrahydropyridazines II-V was isolated from the reaction mixture in 80% yield. The ratio of II-V does not change either during the reaction or during storage, and this constitutes evidence for the absence of interconversions; according to the results of gas−liquid chromatography (GLC), the ratio is 25:17:50:8, respectively. As a result of purification of the mixture by column chromatography, we isolated IV and V in pure form and an inseparable mixture of isomers II and III. (See scheme on next page.)

The results of elementary and spectral analysis of the mixture of II and III and the individual cycloaddition products (IV and V) are in agreement with the Δ^2-tetrahydropyridazine structure. In particular, bands of C=N and C=O bonds are present in their IR spectra (at 1600-1620 and 1730 cm^{-1}), and the UV spectra contain absorption at λ_{max} 240 nm ($\varepsilon \sim 3500$-4000). Singlet signals of a CH_3 group attached to a C=N bond (~1.8-2.0 ppm) and of an acetyl group (~2.0-2.2 ppm), a doublet (J=6.5 Hz) of a methyl group attached to the $C_{(4)}$ atom (~1-1.2 ppm), a septet (J=7 Hz) of the CH portion of a 1-isopropyl grouping (at 3.0-3.5 ppm), and two doublets (J=7.0 Hz) from its diastereotopic methyl groups (~0.8-1.4 ppm) are present in the PMR spectra of

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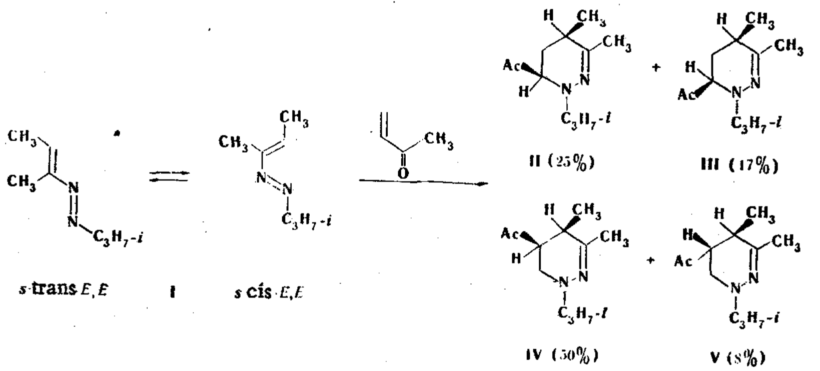
pyridazines II-V. In the spectrum of the mixture of II and III the CH signals of the isopropyl group and of all the CH_3 groups are doubled, and their intensities are in agreement with the GLC data for this mixture.



The fine details of the structures of cycloaddition products II-V can be established from the character of the resonance of the protons in the 5 and 6 positions* if the preferableness of an equatorial orientation of the acetyl group in the 5 or 6 position and stabilization of the pseudoaxial orientation of the 4-CH_3 group due to $A_{1,2}$ strain [5] are taken into account in the half-chair conformation assumed for them. Thus the spectrum of a mixture of II and III contains a multiplet signal of 6-H protons at ~3.4 ppm, and signals are absent at 2.3-3.0 ppm, i.e., the 6 position does not contain a second proton. Consequently, we are dealing with a mixture of cis- and trans-6-acetyl-substituted Δ^2-tetrahydropyridazines. The less intense and weaker-field of the two singlets of the acetyl grouping in the spectrum of the mixture evidently belongs to trans isomer III, in which $A_{1,2}$ strain should be absent in the more stable conformation, and the signal should therefore also belong to the equatorial acetyl group.

The PMR spectra of adducts IV and V do not contain a weak-field signal in the 3.4 ppm region (6-H); however, multiplet signals of the 6-CH_2 group at 2.7-2.9 ppm, augmented by the 5-H multiplet at 2.4 ppm, appeared in place of it.

The multiplet of the 6-CH_2 group in the spectrum of IV is interpreted as the AB portion of an ABX system: H_a 2.77 ppm (J^{gem} = 14 Hz, J^{vic}_{56} = 8 Hz) and H_e 2.89 ppm (J^{gem} = 14 Hz, J^{vic}_{56} = 2.5 Hz). The spin-spin coupling constants (SSCC) correspond, respectively, to $J_{a'a}$ and $J_{e'a}$, and this indicates the stable conformation of the cis isomer of III.

In the PMR spectrum of the trans isomer of V the AB portion of the 6-CH_2 ABX system has the following parameters: H_a 2.74 ppm (J^{gem} = 11.2, J^{vic}_{56} = 5.5 Hz) and H_e 2.84 ppm (J^{gem} = 11.2 Hz, J^{vic}_{56} = 5.0 Hz). In this case the SSCC constitute evidence for averaged values between the $J_{aa'}$, $J_{ae'}$, $J_{ea'}$, and $J_{ee'}$ constants as a result of the contribution of conformations with close stabilities—either with a pseudoaxial 4-CH_3 group or with an equatorial acetyl substituent in the 5 position.

Thus stereospecifity is not achieved in this reaction, but the significant predominance of the cis isomer of IV as compared with stereoisomer V (50 : 8) constitutes evidence for the manifestation of secondary orbital interactions of the acetyl group of the dienophile with the C=C bond of the diene component.

EXPERIMENTAL

The IR spectra of thin layers of the compounds were recorded with a UR-10 spectrometer. The UV spectra of 10^{-4} M hexane solutions of the compounds were obtained with an SF-8 spectrophotometer. The PMR spectra of 10% solutions of the compounds in CCl_4 were recorded with a Varian HA-100 spectrometer with hexamethyldisiloxane as the internal standard.

Analysis by GLC was carried out with a Tsvet-4 chromatograph with a 2 m by 2.5 mm column filled with 5% polyethylene glycol 4000 on Chromosorb W (60-80 mesh) with nitrogen as the carrier gas (90 ml/min) and a column temperature of 160°C. Thin-layer and column chromatography were carried out on activity II Al_2O_3 with elution by petroleum ether–ethyl acetate (7 : 1).

Δ^2-Tetrahydropyridazines II-V. A mixture of 15 g of azo compound I [3], 7 g of methyl vinyl ketone, and 0.1 g of hydroquinone was heated in a sealed ampul at 60°C for one week, after which the volatile components were removed by vacuum distillation, and the residue was chromatographed in 1-g portions with columns filled with

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*The 4-H multiplet is found at 1.7-2.0 ppm and was not reliably localized.

Al_2O_3. The collected fractions were concentrated in vacuo. The mixture of II and III had d_4^{20} 0.9729 and n_D^{20} 1.5018. Found: C 67.4; H 10.2; N 14.2%; MR_D 58.34. Compound IV had d_4^{20} 0.9681 and n_D^{20} 1.4894. Found: C 67.3; H 10.2; N 14.3%; MR_D 58.56. Compound V had d_4^{20} 0.9609 and n_D^{20} 1.4816. Found: C 67.3; H 10.3; N 14.3%; MR_D 58.54. Calculated for II–V: C 67.3; H 10.27; N 14.3%; MR_D 58.54.

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