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ON THE STEREOCHEMISTRY OF BENZYNE ADDITION TO *cis*- AND *trans*-PROPENYL ETHERS[1] AND ACETATES

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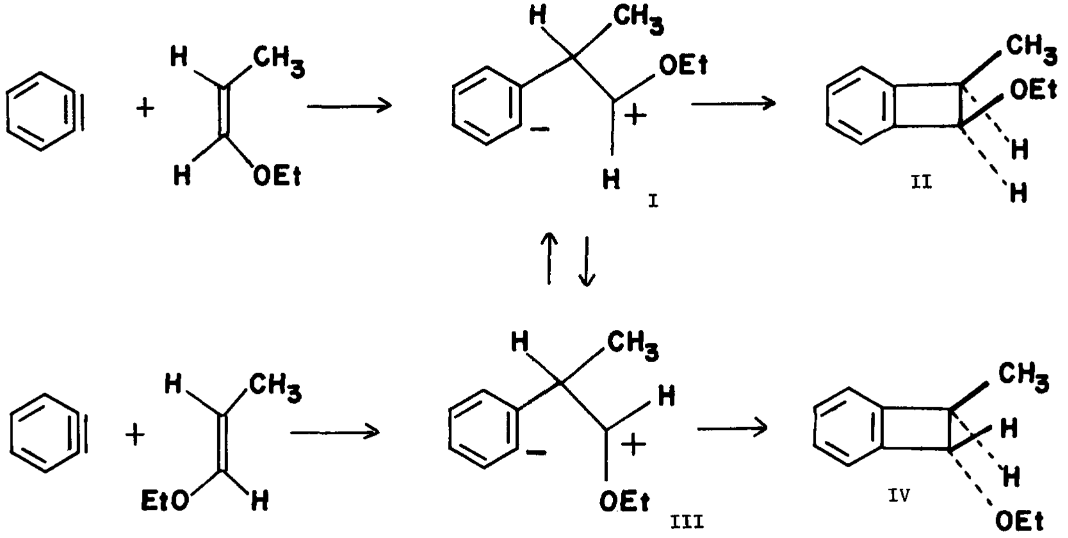
We have recently reported on the reactions of benzyne with electron-rich olefins leading to the formation of benzocyclobutene derivatives.[3] We now describe further studies on these systems which provide information regarding the stereochemical aspects of the cycloaddition. Our findings are in general accord with recent related results of Tabushi and co-workers[4] except for the observation that our substrates, the pure *cis* and *trans* forms of ethyl propenyl ether, undergo a significant amount of competing ene reaction.

The reaction of benzyne (generated from the decomposition of benzenediazonium-2-carboxylate in methylene chloride at reflux temperature[5]) with 100% *cis*-ethyl propenyl ether[6] afforded *cis*-1-methyl-2-ethoxybenzocyclobutene (II, 51%), *trans*-1-methyl-2-ethoxybenzocyclobutene (IV, 3.2%), and ethyl α-phenylallyl ether (V, 0.9%). With 100% *trans*-ethyl propenyl ether, the corresponding reaction with benzyne afforded the *cis* cycloadduct II (8.2%), the *trans* cycloadduct IV (31%), and ethyl α-phenylallyl ether (14%).

cis-1-Methyl-2-ethoxybenzocyclobutene was isolated by preparative vapor phase chromatography (100°)[7] of the reaction mixture from benzyne and *cis*-ethyl propenyl ether; nmr spectrum:[8] τ = 2.91 (singlet, 4H), 5.12 (doublet, J = 4.5 cps, 1H), 6.38 (quartet, 3H), 8.77 (doublet and triplet, 6H); ultraviolet spectrum: λ_{max}^{EtOH} 260mμ (log ε 3.11), 267mμ (3.29), 273mμ (3.28); mass spectrum: parent peak m/e 162. *Anal*. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 80.91; H, 8.72. *trans*-1-Methyl-2-ethoxybenzocyclobutene was isolated by preparative vpc (105°) of the corresponding reaction mixture from *trans*-ethyl propenyl ether; nmr spectrum:[8] τ = 2.92 (singlet, 4H), 5.58 (doublet, J = 1.8 cps, 1H), 6.44 (multiplet, 3H), 8.61 overlap with 8.79 (doublet and triplet, 6H); ultraviolet spectrum: λ_{max}^{EtOH} 260mμ (log ε 3.03), 266mμ (3.22), 272mμ (3.21). Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.60; H, 8.93.

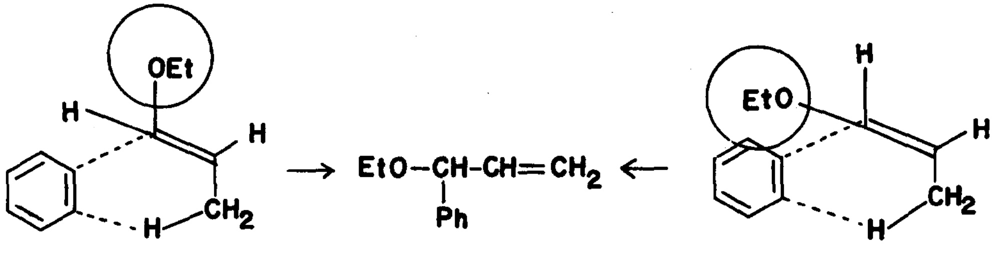
The ratios of cis to trans cycloadducts were determined by integration of the nmr spectra of solutions from which V had been removed.[9] The amount of V formed in each reaction was determined by integration of the vapor phase chromatograph of the product mixtures.[7]



The yields of cis and trans cycloadducts were in the ratio of 94 (II):6 (IV) in the reaction of cis-ethyl propenyl ether and 21 (II):79 (IV) in the reaction of the trans-ethyl propenyl ether. Examination of recovered starting material indicated that no isomerization of the pure ethyl propenyl ethers had occurred. These results lead to the view that the cycloaddition is non-concerted. A similar conclusion has been reached by Jones and Levin in related work on cis- and trans-1,2-dichlorethylene.[10]

We have pictured the reaction as a stepwise process involving dipolar species I and III, although our experimental results do not, of course, exclude diradical intermediates. While the cyclizations are not stereospecific, they are quite obviously stereoselective, indicating that bond rotation in these intermediates is relatively slow compared to ring closure. The fact that there is considerably more ene product in the trans case (14%) relative to cis (0.9%) is in accord with the earlier suggestion by Simmons[11] that this ene reaction is concerted, and sterically inhibited by the interaction of bulky groups with the benzyne ring.

Here, the *trans* orientation of the olefin permits a more favorable geometry of the transition state compared to to the *cis* isomer, as shown:



trans V *cis*

In the case of *cis*- and *trans*-propenyl acetates, both cycloaddition and ene formation were also observed in the benzyne reactions. The overall yields were lower (10-20%) than those obtained with the corresponding ethers, and we again found a predominance of ene reaction with the *trans* isomer. The *cis*-acetate gave a *cis*-*trans* cycloadduct ratio of $\sim$ 3 to 1 while the *trans* isomer gave a *cis*-*trans* ratio of $\sim$ 1 to 2. *cis*-1-Methyl-2-acetoxybenzocyclobutene has peaks in the nmr at τ = 2.84 (multiplet, 4H), 4.09 (doublet, J = 7.0 cps, 1H), 6.12 (multiplet, 1H), 7.79 (singlet, 3H), 8.74 (doublet, J = 7.0 cps, 3H); ultraviolet spectrum: $\lambda_{max}^{cyclohexane}$ 261mμ (log ϵ 3.00), 267mμ (3.23), 273mμ (3.21); *Anal.* Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.93; H, 6.95. *trans*-1-Methyl-2-acetoxybenzocyclobutene was not isolated in a pure state but was identified by the nmr spectrum of the *cis*-*trans* mixture: peaks at τ = 2.81, 4.68, 6.54, 7.99, and 8.57. The ene product, α-phenylallyl acetate, was characterized by independent synthesis from acrolein and phenylmagnesium bromide followed by acetylation; *Anal.* Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.96. Found: C, 75.24; H, 6.70. The *cis*-propenyl acetate reaction mixture yielded chloromethyl benzoate (2.1%) and about 5% of an uncharacterized aromatic solid.

We are exploring further stereochemical aspects of the benzyne-ene reaction with other *cis*-*trans* olefinic systems.

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4. I. Tabushi, R. Oda, and K. Okazaki, *Tetrahedron Letters*, 3743 (1968) studied the reactions of benzyne with pure *cis*-methyl propenyl ether and with various mixtures of *cis*- and *trans*-methyl propenyl ethers. The pure *trans* isomer was not available for their studies. These workers reported that the reaction of benzyne with *cis*-methyl propenyl ether gives benzocyclobutene adducts in the ratio of 86% *cis* to 14% *trans*.
5. The benzenediazonium-2-carboxylate was prepared by a modification of Stiles' original procedure (personal communication from Prof. Stiles). This variant avoids the use of Ag_2O in the workup. cf. L. Friedman, *J. Am. Chem. Soc.*, **89**, 3071 (1967).
6. M. Farina, M. Peraldo, and G. Bressan, *Chem. Ind.* (Milan), **42**, 967 (1960). The isomers were separated by distillation on a Nester Faust all-Teflon Spinning Band column with reflux ratio, 100:1.
7. All vpc work was performed with a 19% fluorosilicone QF-1 on Anakrom ABS column, 11 ft. x 3/8 in.
8. For examples of *cis*-*trans* pairs of benzocyclobutenes in which the proton resonance of the *trans* compound occurs at higher τ values with smaller coupling constants than the related *cis* compound, see H. Hart, J. A. Hartlage, R. W. Fish and R. R. Rafos, *J. Org. Chem.*, **31**, 2244 (1966); G. Fraenkel, Y. Asahi, M. J. Mitchell and M. P. Cava, *Tetrahedron*, **20**, 1179 (1964); A. T. Blomquist and C. G. Bottomley, *Ann.*, **653**, 67 (1962).
9. These figures include a slight allowance, experimentally determined, for the isomerization of the cycloadducts during the removal of V.
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