

PHOTOCHEMICAL 1,3-ADDITION OF ANISOLE TO CYCLOPENTENE.
A STEREOSPECIFIC SYNTHETIC ROUTE TO PERHYDROAZULENES.

R. Srinivasan, V. Y. Merritt, and G. Subrahmanyam
IBM T. J. Watson Research Center
Yorktown Heights, N.Y. 10598, U.S.A.

(Received in USA 9 May 1974; received in UK for publication 18 June 1974)

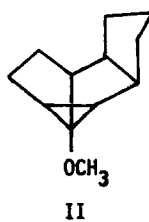
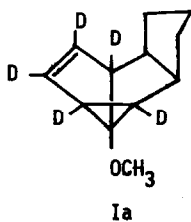
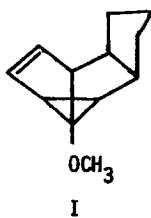
In the seven years that have elapsed since the first report¹ of the photochemical 1,3-addition of benzene to olefins was published, it has been shown that this reaction is a very general one that is applicable to a number of alkylbenzenes as well as to a variety of olefins.² However, the use of this reaction in organic synthesis has been hindered by two factors:

(i) the adducts are susceptible to sensitized decomposition by the aromatic hydrocarbon so that the chemical yields are of the order of 20% or less.

(ii) when many functionally-substituted benzenes were used, the 1,3-mode of addition was negligible or non-existent.³

These shortcomings have now been overcome by the use of anisole as the aromatic reactant. The photochemical additions of anisole to cyclopentene, cyclobutene, and *cis*-3,4-dichlorocyclobutene are predominantly if not exclusively in 1,3-fashion and the chemical yields are high (60-85%). As an illustration of the synthetic utility of this reaction, the 1,3-adduct of anisole to cyclopentene has been transformed in two steps to a perhydroazulene derivative which was the objective of earlier investigations.⁴

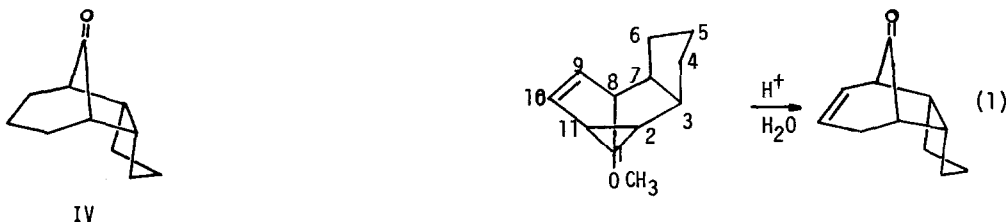
Irradiation of a solution of anisole (2.5M) and cyclopentene (6M) in cyclohexane at 254 nm resulted in the formation of one major product in 85% isolated yield. The product corresponded to a 1:1 adduct.⁵ Its infrared (3010 and 1600 cm^{-1}) and ultraviolet spectra (λ_{max} 220; ϵ_{max} 9400 $\text{l. mol}^{-1} \text{cm}^{-1}$) displayed the absorptions which are typical of the cyclopentene and vinyl-cyclopropane groups in the 1,3-photoadducts of benzene to olefins^{1,2}. The nmr spectrum⁶ of the



compound was consistent with structure I. The protons that were originally on the anisole ring were located by comparing the spectrum of I to Ia, the photoadduct of anisole-2,3,4,5,6-d₅ to cyclopentene. These five proton absorptions (δ 5.64-H₉,H₁₀; 3.10-H₈; 1.95-H₂,H₁₁) were in agreement with typical endo adducts of benzene and alkylbenzenes to cyclopentene.²

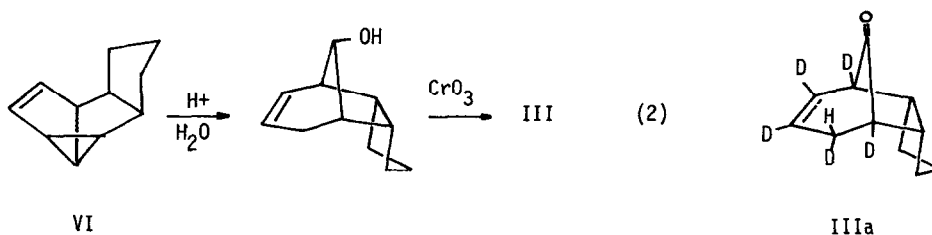
The quantum yield for the formation of I (1.0M cyclopentene; 1.0M anisole in cyclohexane, 254 nm) was 0.17. The high chemical yield in this reaction can be attributed to the stability of the product to sensitized photochemical degradation. This is probably due to the bulk of the -OCH₃ group at C₁ which hinders the approach of a reactant to the cyclopropyl ring. The same effect is also seen in the catalytic hydrogenation (Adam's catalyst-H₂/3.5 atm) as well when only one mole of hydrogen was taken up to yield II.

Refluxing I with HCl in aqueous acetone for 2 hours gave a major product in 80% yield and an unidentified minor product (10%). The major product (mol. formula: C₁₁H₁₄O; b.p. 110° at 0.1 torr) possessed a ketone group (1750 cm⁻¹; $\lambda_{\text{max}}^{\text{pentane}}$ 294 nm; ϵ_{max} 42) with no enolizable hydrogen atoms (treatment with D₂O in the presence of K₂CO₃) and one double bond (1630 cm⁻¹; δ 5.6 2H,m; remaining proton absorptions at 2.3-2.9 6H; 1.36-1.93 6H) and was presumably a tricyclic compound which could be represented as III. On catalytic reduction (Pd-H₂/1 atm) it yielded IV (C₁₁H₁₈O, m.p. 70-71°; 2,4-DNP 108-110°). The formation of III can be via a direct acid cleavage of I or through the transient formation of a cyclopropyl alcohol as an intermediate.

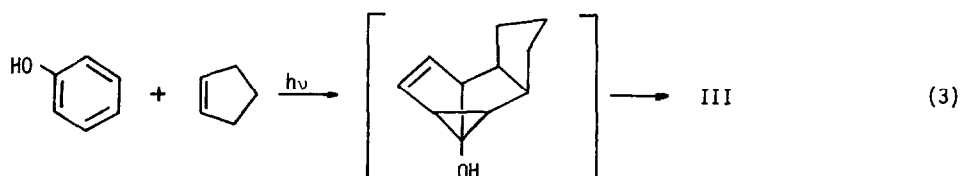


It can be expected from the work of DePuy et al⁷ that, this cleavage would be preferentially at the C₁-C₁₁ bond since C₁₁ is an allylic position. The minor product of this reaction may be the product of C₁-C₂ cleavage but this was not established.

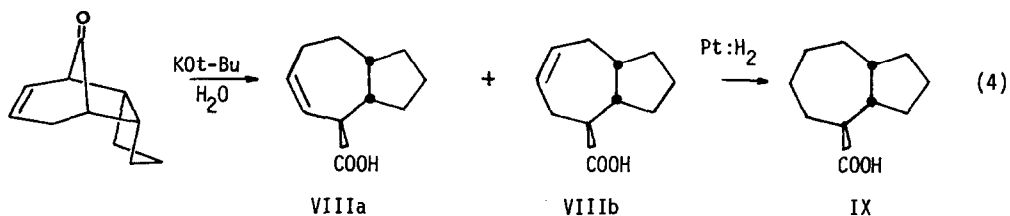
The structure of III was supported by its synthesis via an alternative photochemical route (reaction 2): the endo-1,3-adduct of benzene to cyclopentene (VI) was cleaved with acid to yield the alcohol⁸ which on oxidation with chromium trioxide gave III. The mechanism of the formation of III was investigated in two ways. The acid-catalyzed rearrangement of Ia in an undeuterated medium gave a product (IIIa) which had a single proton absorption at δ 2.78, two protons at 2.39-2.68 while the remaining protons which belong to the cyclopentene methylene



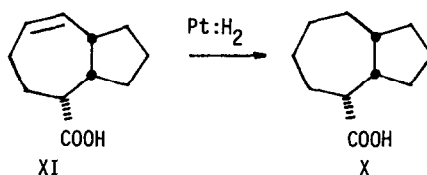
groups were unchanged from III (δ 1.36-1.93). It could also be shown that the photochemical addition of phenol to cyclopentene gave III directly (reaction 3) in low yield. Acid catalyzed rearrangement of II yielded IV (m.p. 70.0-70.5°; 42%).



On stirring III with KOt-Bu/H₂O in ether at room temperature⁹ cleavage of the one-carbon bridge was achieved. The product, VIII (90%, m.p. 57-66°), which analyzed to C₁₁H₁₆O₂ was found to be a mixture of carboxylic acids. It could be catalytically reduced to a single crystalline product IX (m.p. 127-128°) of formula C₁₁H₁₈O₂. Since these transformations were



expected to proceed as in reaction 4, the product IX was compared to X which was made from XI⁴ by catalytic reduction.



IX and X had identical infrared spectra but could be distinguished from their retention times on a Varian FFAP column. Refluxing IX with p-toluene sulfonic acid converted it partly to X

showing that they were epimers. It was therefore possible to compare the nmr spectra of VIII to XI and formulate the former as a mixture of VIIIa and b.

Since the photochemical 1,3-addition reaction is known to proceed with retention of the stereochemistry at the points of addition¹ and since the orientational specificity of the addition allows alkyl substituents to be placed stereospecifically in the adduct¹⁰, this three-step route to perhydroazulenes should prove to be a useful synthetic procedure.

Acknowledgment: The authors wish to thank the Air Force Office of Scientific Research (AFSC), U.S. Air Force for Contract No. F44620-72-C-0024 under which this work was carried out.

References

1. K. E. Wilzbach and L. Kaplan, *J. Am. Chem. Soc.*, **88**, 2066 (1966).
2. V. Y. Merritt, J. Cornelisse and R. Srinivasan, *ibid.*, **95**, 8250 (1973). A complete list of references to earlier work may be found here.
3. Some substituted benzenes such as trifluoromethyl benzene do undergo efficient 1,3-addition. However, the products are not suitable for ready transformation.
4. J. B. Hendrickson and R. K. Boeckman, Jr, *J. Am. Chem. Soc.*, **93**, 1307 (1971) and references therein.
5. All new products gave satisfactory elemental or mass spectrometric analyses.
6. Proton magnetic resonance spectra were determined on a Varian HR-220 spectrometer operated by the Consortium at the Rockefeller University in New York City. Spectra were determined in CCl_4 or $CDCl_3$ solution with TMS as internal reference.
7. C. H. DePuy, G. M. Dappen and J. W. Hausser, *J. Am. Chem. Soc.*, **83**, 3156 (1961); C. H. DePuy and F. W. Breitbeil, *ibid.*, **85**, 2176 (1963).
8. The earlier structure that was reported for this alcohol² has been revised. (*J. Am. Chem. Soc.* in Press).
9. P. G. Gassman, J. T. Lumb and F. V. Zalar, *J. Am. Chem. Soc.*, **89**, 9416 (1967) and earlier references therein.
10. J. Cornelisse, V. Y. Merritt, and R. Srinivasan, *ibid.*, **95**, 6197 (1973).