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INTERNAL DIELS-ALDER REACTIONS IN THE CYCLOPHANE SERIES.
THE REACTION OF A NAPHTHALENOFURANOPHANE WITH DIMETHYL ACETYLENEDICARBOXYLATE

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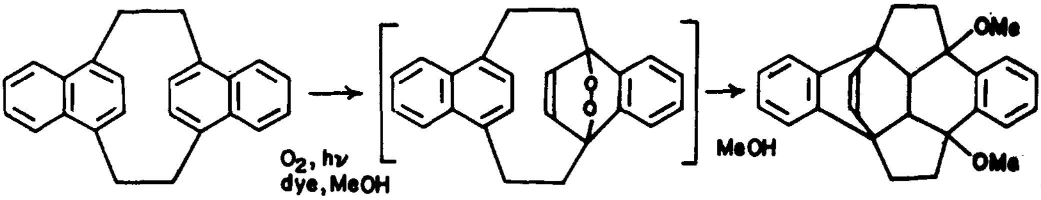
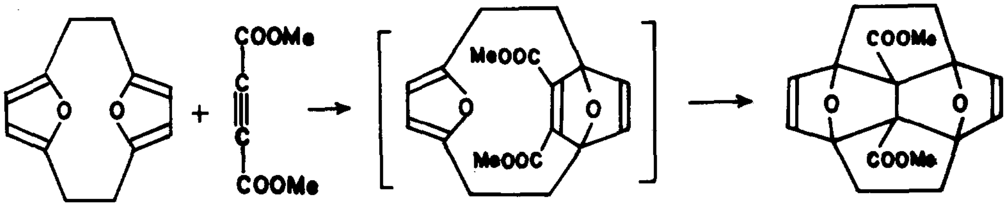
There have been a number of recent reports (1,2,3,4) describing the reactions of cyclophanes with reactive dienophiles whereby initial 1,4-additions are followed by second-stage internal Diels-Alder reactions leading to polycyclic products. This type of cyclization is illustrated below (sequence 1) by the reaction of singlet oxygen with anti-[2.2]-naphthalenophane in methanol (3) and (sequence 2) by the addition of dimethyl acetylenedicarboxylate to [2.2]furanophane (4). We now report a novel example of this type of reaction with a cyclophane containing both naphthalene and furan nuclei. The case described is of particular interest because several modes of cyclization are possible in the second stage.



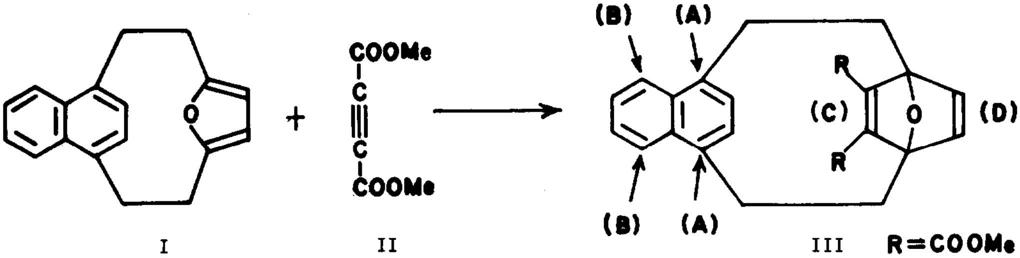
1.



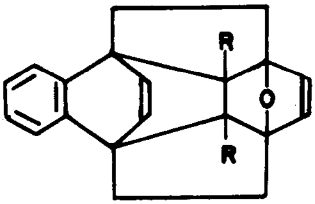
2.

The naphthalenofuranophane (I) (5) was heated in excess dimethyl acetylenedicarboxylate (II) for 20 hr. at 100°. Removal of excess acetylenic ester in vacuo and sublimation of the residue yielded (30%) a crystalline diester m.p. 179°. The new product has weak uv maxima at 278 (ε 1090) and 296 mμ (ε 990) instead of the characteristic strong naphthalene absorption in the starting material at 290 mμ (ε 7,600). Elemental analysis and mass spectral data show that the product has the composition $C_{24}H_{22}O_5$ corresponding to a 1:1 addition product of I and II. Anal. Calcd. for $C_{24}H_{22}O_5$: C, 73.83; H, 5.68. Found : C, 73.59; H, 5.70.

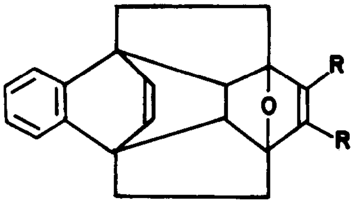
The most reasonable mode of reaction of the above components would consist of an initial Diels-Alder addition of II to the furan moiety of I, forming III, followed by a further (intramolecular) reaction with the naphthalene ring. This second stage reaction is also pictured as a Diels-Alder type of cyclization in which the components are a diene at position A or B, and a dienophile at position C or D. The four possible adducts (not considering stereochemistry) are pictured as IV (A,C addition) V (A,D), VI (B,C), and VII (B,D).



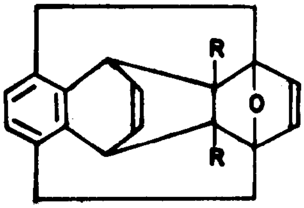
I II III R=COOMe



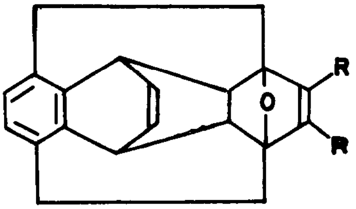
IV (A,C)



V (A,D)

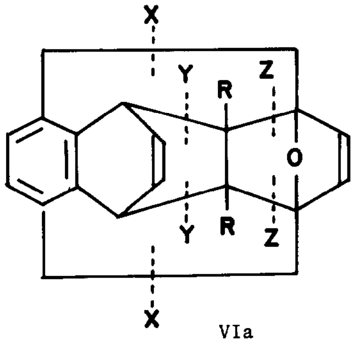


VI (B,C)



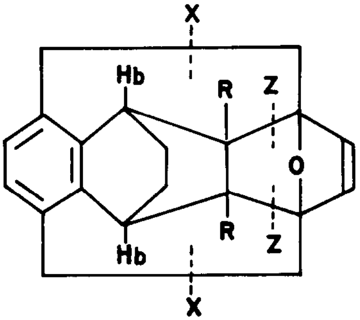
VII (B,D)

Mass spectral information (strong peaks at m/e 390, 296 and 236) indicates that the more reactive dienophile at C rather than the double bond at D is involved in the second-stage reaction (6). Thus, The 296 peak corresponds to the formation of a fragment incorporating naphthalene and acetylenic diester residues (cleavage X,Z) (formula VIa) while the 236 peak is due to a fragment incorporating furan and acetylenic diester residues (cleavage X,Y). This evidence clearly shows that the acetylenic portion of the molecule must be attached to both naphthalene and furan rings, and leaves open to question only the point of attachment of the R-C-C-R residue to the naphthalene ring, i.e., either position A or B, (compounds IV or VI).



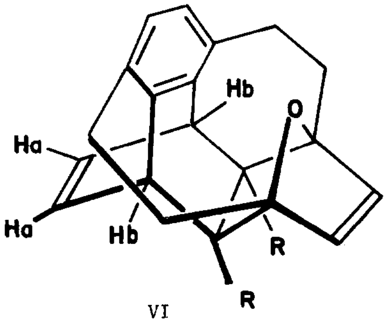
VIa

R = COOMe



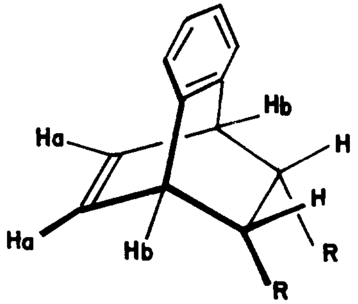
VIII

Of the two remaining possibilities (IV or VI), structure VI (stereochemistry shown below) is clearly favored by the nmr spectrum (7). There are peaks at τ 2.95 (q, 2H), 4.05 (s, 2H), 4.4 (s, 2H), 4.45 (q, 2H), 6.2 (s, 6H), a broad multiplet (8H) between τ 6 and 8 containing a strong peak at 7.5. The lower field quartet (2.95) may be assigned to the olefinic protons Ha, and the higher field quartet (4.45) to the bridgehead protons Hb. Both quartets appear at fields somewhat lower than expected. The splitting pattern of the two quartets is in



VI

R= COOMe



IX

excellent agreement with that observed between Ha and Hb protons in the model benzobicyclo-[2.2.2]octadiene (IX) (8), and does not correspond to the pattern expected for the four protons in the aromatic ring of structure IV.

Confirmation of this assignment was obtained by hydrogenation of the adduct (Pt/C, 2 atm) to form the dihydro derivative $C_{24}H_{24}O_5$ (VIII) (mol. wt. 392, mass spec.). The nmr spectrum of VIII shows that the double bond containing the Ha protons has been saturated (disappearance of the quartet at τ 2.95, and the appearance of a new four-proton broad singlet at 8.3). The bridgehead protons at Hb are now shifted upfield to 5.35 (m, 2H). The mass spectrum of VIII shows, in addition to the parent peak at 392, a strong peak at 298 due to cleavage at X and at Z. Further breakdown of this fragment gives a 270 peak associated with loss of ethylene.

Related Diels-Alder reactions of I with singlet oxygen will be reported separately (9).

Acknowledgments

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6. This finding is in accord with the results of Cram and coworkers (ref. 4) who observed the reaction (sequence 2, above) of the double bond substituted with electron-attracting groups rather than the unsubstituted double bond.
7. The alternative stereoisomer with the oxygen and the double bond of the dihydrofuran ring interchanged is regarded as less likely by analogy with related work (4) and considering the most likely (first stage) mode of addition of the acetylenic diester to the *anti*-form of the [2.2](1,4)naphthaleno(2,5)furanophane (5).
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