Pergamon

Tetrahedron Letters, Vol. 35, No. 24, pp. 4165-4168, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)E0779-W

Synthesis And Diels-Alder Reactions Of A Facially Dissymmetric Tetracyclo-fused Maleic Anhydride With Cyclic Dienes

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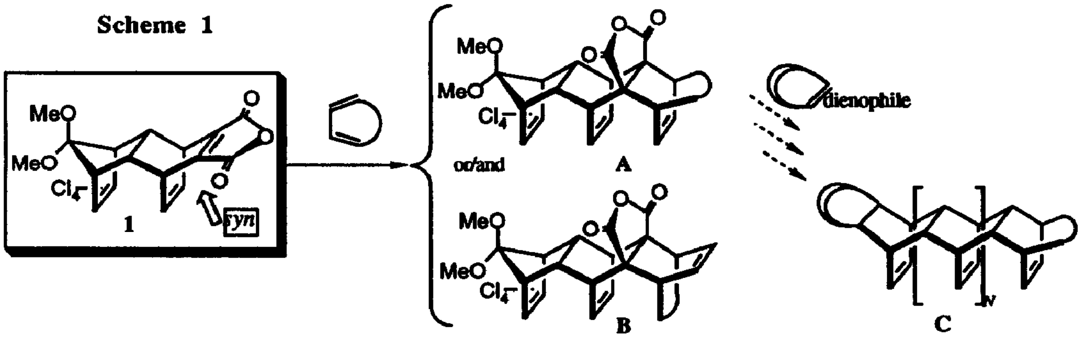
Abstract *:Facially dissymmetric maleic anhydride 1 is synthesized and undergoes Diels-Alder cycloadditions with cyclic dienes exclusively on the face syn to its etheno-bridges.*

The synthesis of rigid polycyclic molecules has continued to play a key role in theoretical organic chemistry by providing rigid and often symmetric frameworks for use as probes to evaluate theories put forth on the physico-chemical properties of organic compounds. For example, synthetic availability of molecule with face-to-face π-systems attached to its rigid molecular backbone has furthered our understanding of intramolecular nonconjugated electronic interactions in terms of through-space and through-bond mechanisms.[1-4] Our interest in the synthesis of rigid polycarbocyclic compounds, particularly those containing π-systems arranged in laticyclic topology [5-7] led us to undertake the synthesis of a facially dissymmetric tetracyclo-fused maleic anhydride 1 (Scheme 1). This compound is of interest not only as a dienophile but also as a cyclic diene for use in Diels-Alder cycloadditions, because it contains an activated double bond and a masked cyclohexadiene moiety which can be generated by a dechlorination-hydrolysis-decarbonylation process.[5-7] We anticipated based upon consideration of steric factors that the [4+2]cyclo-

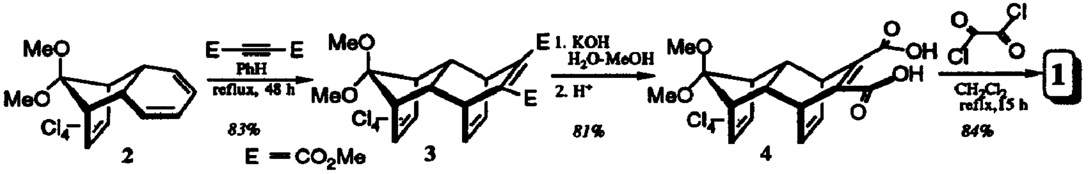
Scheme 1



additions proceed via *syn*-side (relative to the etheno-bridges in 1) attack of the cyclic diene upon 1 to produce *syn-exo* and/or *syn-endo* cycloadducts (A and/or B; Scheme 1). Cycloadducts of the type A could subsequently be subjected to the unmasking of cyclohexadiene substructure (protection of anhydride moiety may deem necessary) for further elaboration of a class of molecules as shown by generic structure C (Scheme 1). In this communication, we report the preperation of 1 and its Diels-Alder reactions with some cyclic dienes; the results of which may offer synthetic entry to structure C.

The synthesis of 1 as presented in **Scheme 2** [8] starts from readily available tricyclic triene 2 [9] following established procedure.[10] Dimethyl acetylenedicarboxylate approached 2 exclusively from the less hindered *exo*-face, as expected by known facts, [5-7] yielding Diels-Alder adduct 3. Dehydration of dicarboxylic acid 4 in refluxing dichloromethane with oxalyl chloride gave anhydride 1 in nearly 60% overall yield from 2.

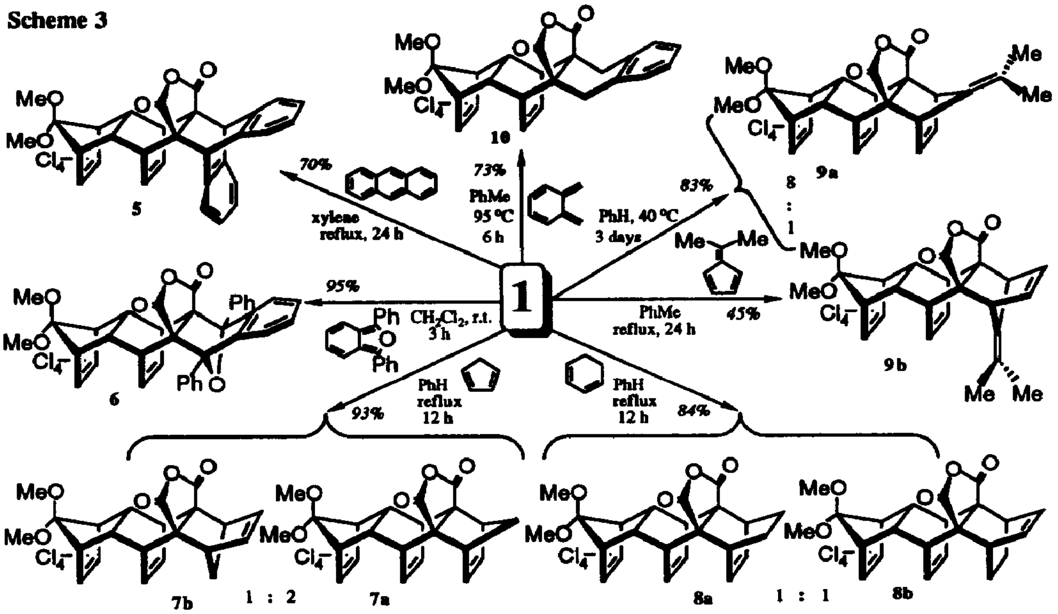
Scheme 2



The maleic anhydride double bond present in 1 readily undergoes Diels-Alder reactions with anthracene, 1,3-diphenylisobenzofuran, cyclopentadiene, cyclohexadiene, 6,6-dimethylfulvene, and *o*-quinodimethane. The results of these cycloaddtions are outlined in **Scheme 3.** [8,11] The reaction of 1 with anthracene in refluxing xylene gave only one of two possible 1:1 adducts in 70% yield after recrystallization from chloroform. Its ^{1}H NMR spectrum, which exhibits a doublet of doublet signal at δ 4.98 due to the vinyl hydrogens of the etheno-bridge as a consequence of a strong anisotropic effect by the proximate benzene ring, suggested 5 as the structure of this adduct.[12] The addition of 1,3-diphenylisobenzofuran to 1 was carried out in dichloromethane at room temperature. Out of the four possible 1:1 adducts, only one adduct was obtained in 95% yield. The respective upfield chemical shift of δ 5.68 (dd) for etheno-bridge hydrogens and the broad singlet at δ 2.76 (nearly same as that in 5; δ 2.78) due to tertiary hydrogens at ring fusion in the ^{1}H NMR spectrum of this adduct led us to suggest the structure 6 which resulted from *syn*-side attack of 1,3-diphenylisobenzofuran upon 1 and *endo*-addition in accordance to Alder rule.[13]

The cycloaddition of 1 with cyclopentadiene in refluxing benzene afforded two 1:1 adducts in a ratio of 2 to 1 (total yield 93%). The *syn,exo*-structure 7a is assigned to the major adduct, for among four possible isomeric adducts only 7a is expected to display in its ^{1}H NMR spectrum the absorption signals at δ 5.71 (t) and δ 5.52 (dd) for vinyl protons of the etheno-bridges, indicating consequences of three proximal face-to-face oriented etheno-bridges.[14] In the ^{1}H NMR spectrum of minor product, these two groups of etheno-bridge hydrogens appeared at δ 6.43 (t) and δ 6.13 (dd), revealing all three other isomers were possible. The information that led us to suggest 7b as the structure of this minor adduct came from the large difference of chemical shifts ($\Delta\nu$ = 1.51 ppm) displayed by two protons at the methano-bridge.[15] Similarily, cyclohexadiene added to 1 forming two isomeric 1:1 adducts of equal amount in 84% total yield. One of the adducts, which displayed signals for hydrogens of etheno-bridges at δ 5.88 (dd) and δ 5.72 (dd) in its ^{1}H NMR spectrum, could be consistent only with the structure 8a arising from a *syn* and anti-Alder-rule attack on 1 by

Scheme 3



cyclohexadiene. In the ^1H NMR spectrum of the other adduct, the hydrogens of two etheno-bridges appeared at δ 6.35 (dd) and δ 6.10 (dd). This information, together with the results from the NOE-difference spectral analysis,[16] led us to suggest strucutre **8b** for this adduct. The reaction of **1** with 6,6-dimethylfulvene in refluxing toluene produced a single adduct in 45% yield. This adduct was also obtained, but in only 9% yield, from the reaction which was carried out at 40 °C in benzene as solvent. The major adduct [17] produced in 74% yield was identified to be **9a** as evident from the absorption signals at δ 5.83 (t) and δ 5.55 (dd) due to vinyl protons of the etheno-bridges in its ^1H NMR spectrum. The ^1H NMR spectrum of the minor adduct, which displayed absorption signals of at δ 6.43 (t) and δ 5.81(dd), together with the NOE-difference spectral analysis[16] led us to suggest **9b** as the structure of this adduct. When **1** was subjected to the reaction with *o*-quinodimethane generated in situ from pyrolysis of 1,4-dihydro-2,3-benzoxathin, [18] only one of the two possible isomeric 1:1 adducts was obtained in 73% yield. Based on the the NOE-difference spectral analysis,[16] structure **10** was assigned to this product.

In summary, the facially dissymmetric maleic anhydride **1** exhibits high π-facial selectivity in the Diels-Alder cycloadditions by adding to cyclic dienes exclusively with its face *syn* to the etheno-bridge. The anhydride moiety in **1** does not seem to strongly direct the additions to proceed by Alder's rule to yield the adducts as depicted by structure **B** in Scheme 1.[19] An effort directed toward the understanding of factors which determine the π-facial selectivity of **1** is undertaken. Work directed toward the exploitation of the synthetic application of **1** is also in progress.

Acknowledgment. This work has been supported by the National Science Council of the Republic of China.

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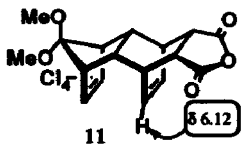

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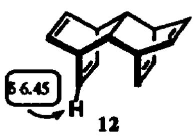

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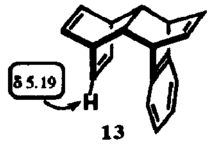

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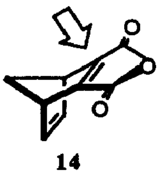

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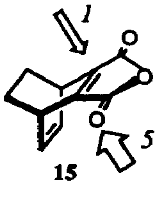

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(*Received in Japan* 5 *November* 1993; *accepted* 10 *March* 1994)