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TORSIONAL ANGLE DECOMPRESSION IS NOT THE SOURCE OF FACIAL SELECTIVITY IN DIELS-ALDER CYCLOADDITIONS INVOLVING CYCLIC DIENES FUSED TO BICYCLIC FRAMEWORKS. THE CASE STUDY OF 1,2,3,4,6,7-HEXAHYDRO-1,4-METHANONAPHTHALENE

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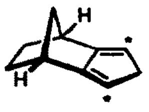
Abstract: Hydrocarbon **3** has been synthesized and shown to enter into Diels-Alder cycloaddition preferentially from the top face. This behavior, and that of **2**, cannot be accounted for in terms of torsional strain minimization.

The kinetic preference exhibited by isodicyclopentadiene (**1**) for below-plane dienophile capture is striking[1] because bonding takes place from the sterically more hindered π-surface.[2] This facial selectivity was interpreted by Paquette and Gleiter to be a consequence of disrotatory orbital tilting within Ψ_1 induced by admixing of the high-lying norbornyl σ-orbitals with the proximal π orbitals of the diene.[3] Destabilizing antibonding interactions are minimized when the 2π reactant approaches from the bottom. More recently, Brown and Houk advanced an alternative explanation for this phenomenon based on an MM2 model.[4] In their view, below-plane attack of a dienophile (ethylene) is favored because the torsional angle between the asterisked sp^2-hybridized carbons and the bridgehead hydrogens in the affiliated transition state is larger (26.6°) than that associated with approach from the top (14.7°). A strain energy difference of 0.6 kcal/mol favoring the below-plane transition state was proposed.



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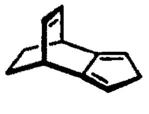

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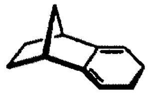

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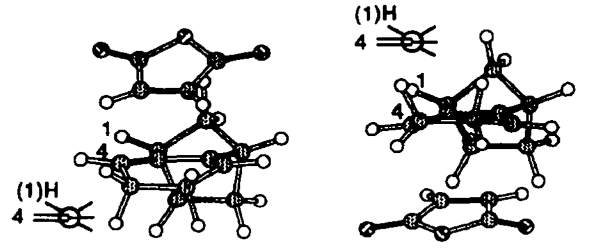
This analysis was considered by us to warrant further investigation since the cycloaddition behavior of **2**, a hydrocarbon studied by us alongside **1**, did not conform to these guidelines.[1b,3a,5] Dienophiles add to **2** predominantly from the above-plane direction (79-100%). In this system, the key torsional angles at the same point in the reaction trajectory, *viz.*, 8.5° (bottom) and 2.4° (top) for maleic anhydride as the dienophile (Table I), would require fundamental adherence to facial selectivity identical to that operational in **1**. At the experimental level, this is not seen. Consistent with this behavior, however, is the release of ring strain within the bicyclic subunit present in **2** and attendant lowering of σ-orbital energies to a considerable degree. As a result, the σ/π gap is now too large for significant interaction to materialize and the π-orbitals are no longer tilted. Consequently, prevailing steric effects become controlling of stereoselectivity.

Table I. Calculated Transition StateTorsional Angles for the Diels-Alder Addition of Maleic Anhydride to 1-3.[a]

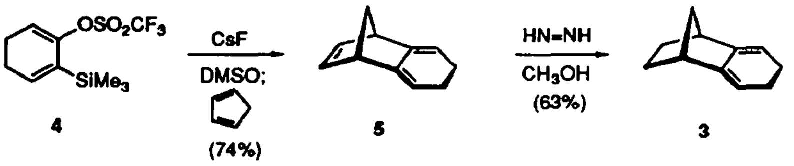
Compd	top-face, endo	bottom-face, exo
1	20.1°	26.2°
2	2.4°	8.5°
3	18.6°	26.8°

[a] The torsional angles in question are defined in the drawings for 3 to the right.



There is general accord that other avenues are available for relieving the strain present in 1.[6,7] One option is to increase the size of the fused ring as in the title compound 3. Widening of the angles internal to the pendant ring serves to ameliorate σ/π interaction sufficiently to eliminate orbital tilting as an operational controlling element. Therefore, dienophiles should attack the more open exo face of 3 stereoselectively. Adherence to the Brown/Houk hypothesis would require, however, that approach from below-plane be favored since the torsional angle associated with this pathway (26.8°) is significantly less constraining than that associated with topside approach (18.6°).

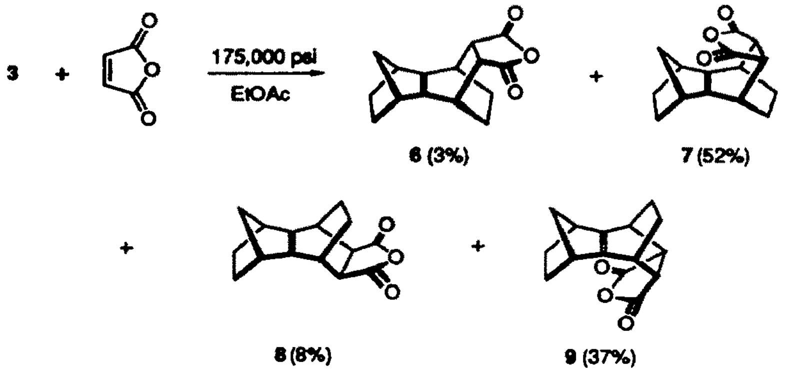
Scheme I



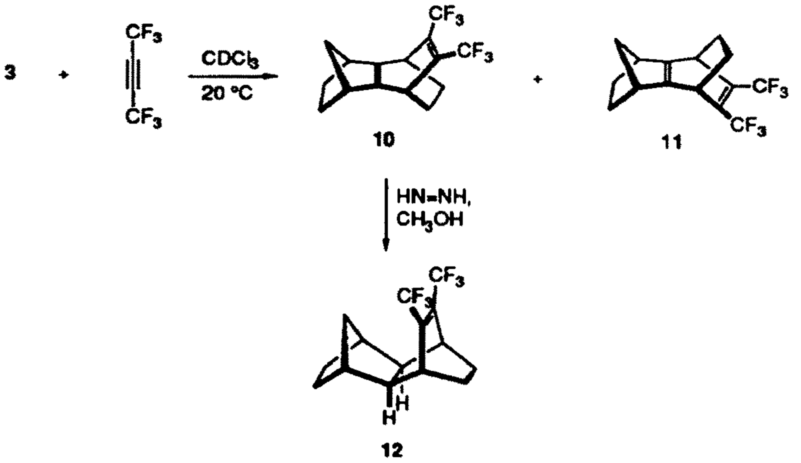
To resolve this issue, 3 was prepared by the route outlined in Scheme I. In 1990, Shakespeare and Johnson reported that 1,2,3-cyclohexatriene could be generated in solution and trapped with diphenylisobenzofuran.[8] In an adaptation of their procedure, dienyl triflate 4 was treated with cesium fluoride in dry DMSO just prior to the introduction of cyclopentadiene. Since triene 5 produced in this manner proved to be rather labile, its reduction with diimide was performed without delay. Hydrocarbon 3 was obtained as a colorless oil exhibiting characteristic ^{1}H [(200 MHz, $CDCl_3$) δ 5.32 (s, 2 H), 2.75 (s, 2 H), 2.14 (m, 4 H), 1.66 (m, 2 H), 1.35 (m, 4 H)] and ^{13}C NMR spectral features [(50 MHz, $CDCl_3$) ppm 143.7, 110.5, 42.2, 40.7, 28.9, 22.8].

Although 3 proved to be very selective in the dienophiles with which it would react,[9] cycloaddition occurred in the presence of maleic anhydride under high pressure conditions during 4 days. All four possible adducts resulted. Nuclear Overhauser procedures established that major product 7 was the result of top-face, endo attack. The secondmost prevalent isomer was identified as 9 by similar techniques. Although the 6/8 pair of anhydrides proved inseparable, their presence in a 1.0:3.1 ratio was spectroscopically evident.

With hexafluoro-2-butyne as co-reactant, cycloaddition in $CDCl_3$ proceeded to the 63% level

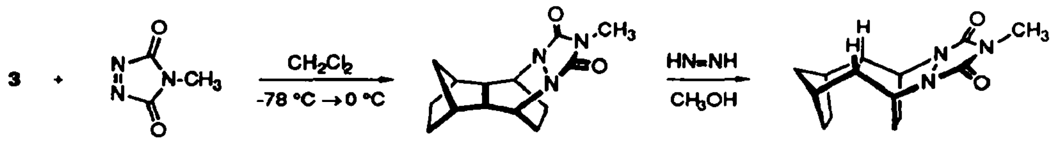


after 72 h. ^1H NMR analysis of the reaction mixture revealed that two cycloadducts had formed in a ratio of 4.3:1.0 by integration of new absorptions at δ 3.97 and 4.02, respectively. Following chromatographic separation, the major isomer was subjected to diimide reduction. NOe studies performed on **12** corroborated not only that it had been formed from **10**, but that the stereochemical course of this reduction was rather unusual.



The Diels-Alder reaction between **3** and N-methyltriazolinedione was complete within a very short time. In this instance, adduct **13** was formed quantitatively. When exposed to diimide as before, reduction occurred to provide **14**. Spectroscopic studies performed on this dihydro derivative confirmed that the triazolinedione and diimide had both added to the top face of the diene and cycloadduct, respectively.

The top-face bias observed for dienophilic capture by **2** and **3** contrasts with that exhibited by **1**. Since all three substrates have transition structures in which torsional strain is calculated to be heightened during attack from above-plane,[10] steric contributions of this type are clearly too small to impact significantly on cycloaddition stereoselectivity. The Brown-Houk proposal suggesting that the origin of π-facial selectivity lies exclusively in torsional effects is therefore unsuitable as a predictor of



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cycloaddition stereochemistry. On the other hand, our original explanation that σ/π interaction generated uniquely in highly strained frameworks influences stereoselection because of π-orbital tilting is in good agreement with the experimental data. The extent to which σ/π interaction serves to concisely rationalize the course of other stereoselective reactions should be construed to be an indication that stereoelectronic control is a force with which to be reckoned.[11]

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