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π-FACIAL STEREOSELECTIVITY IN THE DIELS-ALDER REACTION - III.[1] AN UNSYMMETRICALLY BIRDCAGE-ANNULATED CYCLOHEXADIENE

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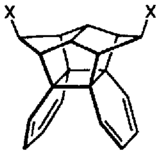
Abstract *The steric environment within diene **2** is shown to direct attack of ethylenic, acetylenic and heterodienophiles predominantly from the* syn *π-face.*

syn-o,o-Dibenzene derivatives **1** serve as building blocks in our pagodanes → dodecahedranes syntheses[2] In the course of investigations on the π-face selectivity of dienes **1** in domino and pincer Diels-Alder cycloadditions, we noted a significant bias in their reactivity against certain dienophiles due to the specific *vis-a-vis* orientation of the two diene moieties[1] As a test for dienophile capture in the absence of possible cooperative effects, the behavior of the simpler cyclodiene[3] **2** was scrutinized



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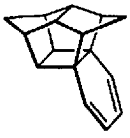

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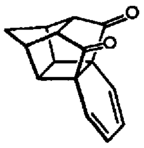

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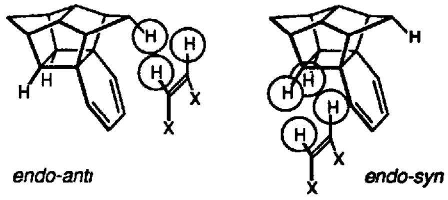
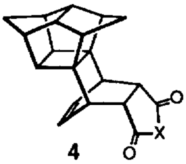
Factors controlling the stereoselectivity of [4+2]-cycloaddition reactions beyond effects covered by FMO theory,[4] *i e* second-order orbital interactions *vs* subtle steric influences, enjoy continuous attention[5-8] Whereas for the polycyclic diketodiene **3**, to name a structurally related case, secondary carbonyl orbital and steric effects have been shown to act cooperatively in the addition of most types of dienophiles,[8] electrostatic or extended π-interactions are absent in rigid hydrocarbon **2** what allows a detailed assessment of steric factors Directive influences from σ/π-mixing[5] operative between olefinic and Walsh orbitals of the fused cyclobutane ring[9] are considered to be less important For the polycycle **2**, a different degree of steric interference between the reactants can be anticipated for the two modes of attack to the dissymmetric π-faces, defined in Fig 1 as "*anti*" or "*syn*" relative to the four-membered ring For steric reasons, high *endo* selectivity is generally expected

Figure 1. Crucial steric interactions for the *endo* attack modes of *cis*-substituted ethylenic dienophiles toward **2**



The details and results of our study with **2** are compiled in Table I This diene expectedly proved to be much less reactive than 1,3-cyclohexadiene Consequently, our investigation was restricted to the most reactive dienophiles to guarantee conditions of kinetic control Conversions were followed by t l c and proton NMR Crude reaction mixtures were analyzed by high-field ^{1}H NMR and product ratios determined by integration of the well-resolved olefinic proton signals for the resulting bicyclic [2 2 2] moieties Stereochemical determinations were facilitated in that the proton signal for the unsaturated bridge of *syn*-adducts was generally observed at higher field ($\Delta\delta$ 0 2-0 3 ppm) relative to that of corresponding *anti*-adducts (Table I) For selected cases, NOE and spin-decoupling experiments were used to secure the assignments



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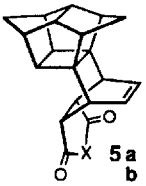
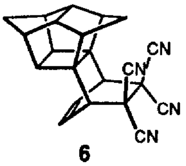


5a X=O
b X=N-Ph



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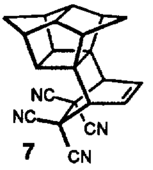

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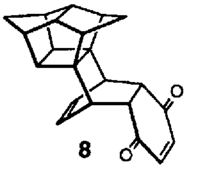

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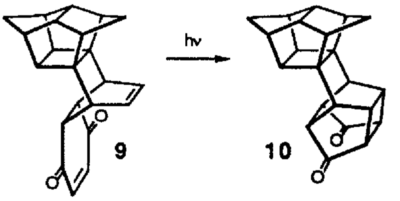


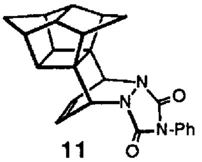
Addition of ethylenic dienophiles like maleic anhydride, N-phenylmaleimide and benzoquinone produced mixtures of *anti*- and *syn*-stereoisomers **4a**/**5a**, **4b**/**5b**, and **8**/**9** respectively, with *syn*-regiochemistry dominating (Table I) [10] In case of *syn*-isomer **9**, photochemical cyclization into cage diketone **10** confirmed the *endo* stereochemistry Even in the reaction with tetracyanoethylene the *syn*-addition path predominates by far (**6** **7** = 6 94), although it seems to be the sterically more congested one The tetrasubstituted dienophile, however, required prolonged heating in refluxing toluene for complete addition While the above NMR criteria in this case are ambiguous, stereochemical differentiation is secured by the significant low-field shift (ca 1 ppm) for the cyclobutane proton signal of the major component — a consequence of the spatial proximity of these hydrogens with the nitrile groups

The highly reactive, sterically less demanding heterodienophiles N-phenyltriazolinedione and singlet oxygen were captured almost exclusively from the *syn*-π-face of **2** to yield urazole **12** and endoperoxide **16**, with only traces (≤ 2%) of the *anti*-isomers **11** and **15** being detectable Endoperoxide **16** rearranges into diepoxide **17** at temperatures >110°C [11] Reaction with nitroso-

Table I. Reaction Conditions and Product Ratios for Cycloadditions to 2[10]

Reagent	Products (*anti/syn*)	δ ($CDCl_3$)	Ratio	Yield (%)	Conditions
maleic anhydride	**4 a + 5 a**	6 43, 6 19	12 . 88	95	benzene, 4 h, 80°C
N-phenylmaleimide	**4 b + 5 b**	6 39, 6 16	10 : 90	95	toluene, 8 h, 80°C
p-benzoquinone	**8 + 9**	6 34, 6 09	18 : 82	85	toluene, 5 h, 100°C
tetracyanoethylene	**6 + 7**	6 79, 6 53	6 : 94	95	toluene, 4 5 h, 110°C
N-phenyltriazolinedione	**11 + 12**	6 60, 6 39	2 · 98	100	CH_2Cl_2, 0°C
singlet oxygen	**15 + 16**	6 77, 6 58	1 99	80	benzene, 2 h, 80°C
dimethyl acetylenedicarboxylate	**18 + 19**	6 52, 6 25	2 98	80	neat, 1 h, 100°C
dicyanoacetylene	**20 + 21**	6 51, 6 24	2 · 98	95	toluene, 4 5 h, 100°C

benzene was the only one found to be reversible under the conditions employed (benzene, 80°C) Initially, *syn*-adduct **14** predominates as expected (**13**/**14** ≈ 1.3 at 20% conversion)



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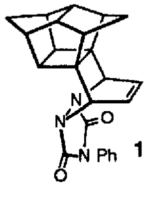

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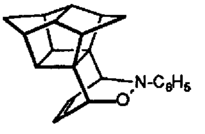

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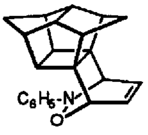

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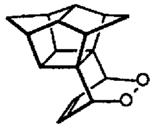

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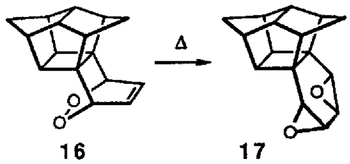
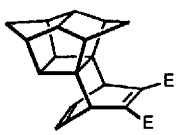


16 **17**

Reactive acetylenic dienophiles such as dimethyl acetylenedicarboxylate or dicyanoacetylene were both engaged in [4+2]-addition with high π-facial stereoselectivity (98% **19**/**21**)[12]



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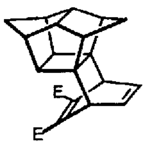

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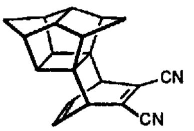

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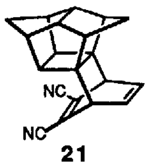

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Obviously, [4+2]-cycloaddition to **2** proceeds for all types of dienophiles with overwhelming kinetic preference for approach from the cyclobutane fused, *syn*-diene face[13] This high π-facial stereoselectivity has to be attributed to the relative magnitude of nonbonded steric repulsions during dienophile capture, where the opposing methylene bridge causes the more effective shielding — a view strengthened by the somewhat reduced selectivity for ethylenic cycloaddends which can be rationalized by the pronounced steric interaction for the *syn*-trajectory (Fig 1) Steric requirements for all "non-hydrogen bearing" dienophilic reactants tested (acetylenes, heterodienophiles) seem to be of comparable magnitude At present, however, it cannot be convincingly ruled out that the latter types might additionally benefit from some degree of secondary orbital effects,[8b] especially as for the reactive 2π-components employed consequences of an early transition state have to be considered[6]

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References and Notes

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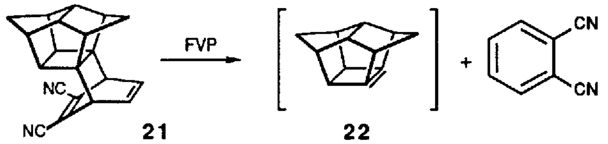
10 Reactions were conducted on a 0 1-0 3-mmol scale with 10-fold excess of dienophiles. Crude adduct mixtures were analyzed by ^{1}H NMR prior to purification by either recrystallization or LC All major components are fully characterized by their spectra (^{1}H, ^{13}C NMR, IR, UV, MS) and elemental analysis, Grund, C *Dissertation,* University of Freiburg 1990

11 [2 1 1]-*cis*-Dioxa-tris-σ-homobenzenes such as **17** undergo an alternative [$\sigma2+\sigma2+\sigma2$]-cycloreversion – if at all – only at much higher temperatures Prinzbach, H , Maas, M , Fritz, H , McMullen, G *Tetrahedron Lett* **1980,** *21,* 4897-4900

12 The value of these products as potential precursors to the corresponding highly pyramidalized cage olefin **22** (cf Borden, W T *Chem Rev* **1989,** *89,* 1095-1109) via benzenoid [4+2]-cycloreversion has yet to be determined So far, complete conversion of **21** upon FVP at 500°C was noted providing a near quantitative yield of 1,2-dicyanobenzene



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