Tetrahedron Letters,Vol.30,No.24,pp 3133-3136,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
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DOMINO AND PINCER CYCLOADDITIONS WITH *syn-o,o'*-DIBENZENES SCOPE AND π-FACIAL STEREOSELECTIVITY

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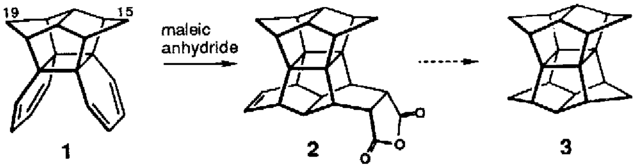
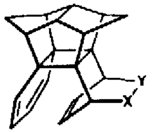
Summary: *The syn-o,o'-dibenzene units in 1 and 5 capture a range of (hetero)ethylenic dienophiles with complete outside, acetylenic dienophiles with changing preference.*

The Diels-Alder addition of maleic anhydride (MA) to the remarkably thermally stable *syn-o,o'*-dibenzene derivative **1** is a key step in our synthesis of pagodanes (**3**),[1] advanced precursors in our quest for dodecahedranes.[2,3] The addition was found to proceed stereospecifically to yield quantitatively the polycondensed domino[4] adduct **2** resulting from an outside attack.



In order to evaluate the scope of this reaction for preparative applications, a systematic study was undertaken with special attention given to the conceptual intermediacy of primary cycloadducts of type **4**[2] in which an exceptionally close relationship between diene and dienophile (ca. 3 Å) is enforced. Further disclosure of the structural and stereoelectronic prerequisites for this type of multiple cycloaddition reactions was expected from a comparison with dibenzo analogue **5**.[2,5] Mechanistic considerations about the origin of the π-facial stereoselectivities are detailed in the subsequent letter.[6]



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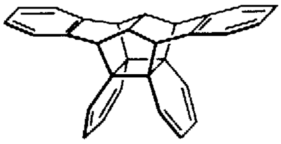

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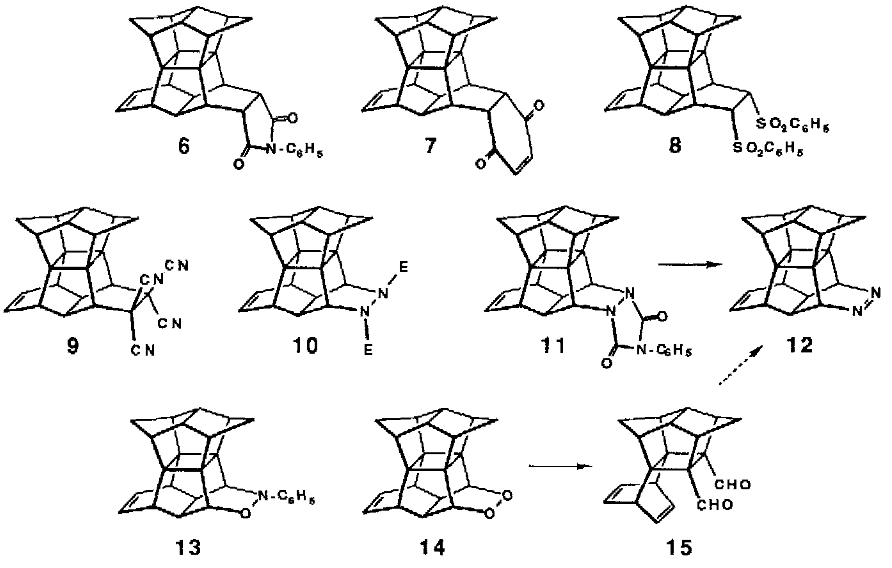
Although the diene units in **1** are established as being electron-rich because of extensive through-bond coupling and σ/π-orbital mixing,[7] the addition of MA requires elevated temperatures (80°C), primarily due to steric hindrance through the 15-/19-*syn* protons (X-ray analysis[1]) which impede the contiguous outside approach of the dienophile. In view of the limited thermal stability of tetraenes **1** and **5** ($t_{1/2}(120) \approx 130$ and 10 min),[8] dienophiles of low reactivity had to be presumed unsuitable. While an attack of ethylenic dienophiles into the cleft formed by the cyclodiene moieties is *prima facie* relatively unlikely, this type of capture is more conceivable with acetylenes (pincer addition[4]) or hetero-dienophiles.

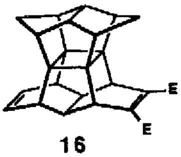
For the cycloadditions reported in this study, the reaction conditions and product ratios are summarized in Table I.[9] From a variety of ethylenic dienophiles, with N-phenylmaleic imide (**6**), *p*-benzoquinone (**7**) and *(Z)*-1,2-bis(phenylsulfonyl)ethylene (trace amounts of **8**) could formation of product be noted alongside increasing competition from [6+6]-cycloreversion. The highly reactive corresponding *(E)*-bissulfone could not be engaged in [4+2]-addition presumably due to adverse steric interaction of one of the bulky substituents. No addition took place with less reactive reagents[10] such as acrylic acid derivatives or phenyl vinyl sulfoxide (sulfone) at temperatures up to 180°C. In analogy to the established stereochemistry of **2**,[1] an *endo*-configuration was secured for the adducts by NOE experiments.



Diethyl azodicarboxylate only sluggishly entered into reaction (**10**; *trans*-configuration according to ^{1}H NMR); in view of the results for the *(E)*- and *(Z)*-bissulfone pair, presumably a *trans*→*cis* isomerization has to precede the cycloaddition. In contrast, N-phenyltriazolinedione (NPTD) proved extremely reactive towards **1**. The resulting urazol **11** serves as convenient precursor for azo-[2.2.1.1]pagodadiene **12**. Nitrosobenzene required elevated temperatures for addition (**13**) to take place. Endoperoxidation (**14**), when conducted at higher temperatures, was accompanied by partial decomposition into dialdehyde **15**. It remains to be tested whether **15** can qualify as alternative precursor for **12** upon hydrazine treatment.[11] On account of strong steric inhibition, tetracyanoethylene mechanistically shows borderline behavior and only at 110°C is its dienophilic reactivity (**9**) sufficient to override competition from catalyzed symmetry-forbidden $2\sigma\rightarrow2\pi$-cleavage[8] of **1** to the isomeric dibenzo compound. The latter transformation is exclusively induced by the electrophilic dienophile chlorosulfonyl isocyanate.

All above dienophiles are engaged in π-facially stereospecific outside additions to **1**. No indication for regioisomeric inside capture of these dienophiles could be found, even for sterically undemanding heterodienophiles like NPTD, over a temperature range from -100 to +140°C. Likewise, under no experimental conditions could a hypothetical primary adduct of the type 4 be detected or intercepted before a consecutive intramolecular [4+2]-step, *e.g.* with a huge excess of dienophile in the reaction with NMTD at -100°C.

As anticipated, with sterically less demanding acetylenic reagents, a competitive inside capture of the dienophilic moiety indeed leads to formation of C_{2v}-symmetrical pincer products, ranging from 3% **17** with dimethyl acetylenedicarboxylate (DMAD) to up to 74% **19** with dicyanoacetylene (DCA). Even under forcing conditions, no cycloadduct was formed with methyl propiolate or tosyl acetylene.



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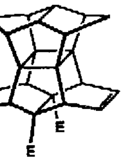

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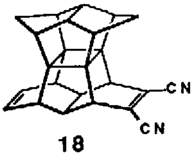

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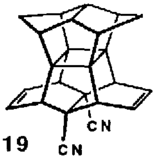

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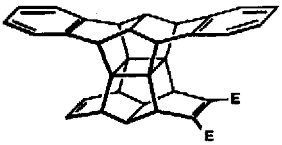

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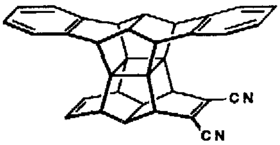

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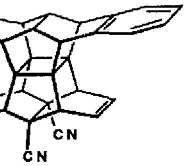

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Table I. Reaction Conditions and Product Ratios for Cycloadditions with 1 and 5.

Reagent	Domino/pincer ratio		Yield (%)	Conditions[a]
	1	5		
maleic anhydride	100 : 0	100 : 0	100/95	80°C, 12 h/110°C, 4 h
N-phenylmaleimide	100 : 0	100 : 0	100/90	80°C, 30 h/100°C, 4 h
p-benzoquinone	100 : 0	100 : 0	79/85	100°C, 24 h/100°C, 4 h
(Z)-1,2-bis(phenylsulfonyl)ethylene	100 : 0	-	traces/-	140°C, 24 h/-[b]
tetracyanoethylene	100 : 0	-	40/-	140°C, 8 h/-
N-phenyltriazolinedione	100 : 0	100 : 0	100/100	0°C, instant./0°C, instant.[c]
singlet oxygen	100 : 0	100 : 0	43/50	80°C, 2 h/56°C, 2 h
nitrosobenzene	100 : 0	100 : 0	82/85	80°C, 4 h/100°C, 4 h
dimethyl acetylenedicarboxylate	97 : 3	100 : 0	89/traces	100°C, 80 h/120°C, 4 h[d]
dicyanoacetylene	26 : 74	88 : 12	70/75	100°C, 4 h/100°C, 4.5 h

[a] Reactions were conducted in benzene or toluene on a 0.1-1.6-mmol scale with 10-fold excess of dienophiles.

[b] 1,2-dichlorobenzene [c] dichloromethane [d] neat

Dibenzotetraene **5** proved to be slightly less reactive than **1** although the outer diene faces appear to be sterically more accessible. (Hetero)ethylenic dienophiles furnished domino-type adducts stereospecifically. From the reaction with DMAD, only the domino product (**20**) was formed, whereas DCA yielded a minor amount of a pincer compound (**21**:**22** = 88:12) upon thermal activation.[6] Especially with less reactive dienophiles, considerable amounts of janusene arose from retrograde [6+6]-competition due to the lower Diels-Alder reactivity and lower thermal stability of 5. Thus, its preparative value as a benzo[2.2.2.2]pagodane synthon[5] clearly is restricted to highly reactive reagents.

Acknowledgement: Financial support by the *Deutsche Forschungsgemeinschaft*, the *Fonds der Chemischen Industrie*, and the *BASF AG* is gratefully acknowledged.

References and Notes

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9) Crude adduct mixtures were analyzed by ^{1}H NMR prior to purification either by recrystallization or LC. All major components are fully characterized by their spectra (^{1}H, ^{13}C NMR; IR; UV; MS) and elemental analysis; *e.g.* **16**: ^{1}H NMR ($CDCl_3$) δ 6.11 (dd,2H), 3.78 (s,6H), 3.20 (m,2H), 2.84 (m,2H), 2.62 (m,2H), 2.23 (m,2H), 2.18 (m,2H), 2.00 (m,2H), 1.46, 1.45, 1.36, 1.30 (2 AB sets,4H). **19**: ^{1}H NMR ($CDCl_3$) δ 6.38 (dd,4H), 3.30 (m,4H), 2.64 (m,2H), 2.28 (m,4H), 1.50, 1.32 (AB,4H); ^{13}C NMR (C_6D_6) δ 130.4, 119.5, 59.9, 57.8, 57.7, 43.1, 42.6, 40.8.
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(Received in Germany 28 March 1989)