

π -Facial Stereoselectivities in Diels–Alder Cycloadditions to a Dissymmetric Cyclohexa-1,3-diene Moiety in a Novel, Caged Polycyclic Framework

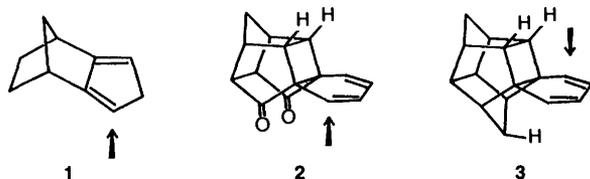
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Novel polycyclic 1,3-dienes **4** and **5** have been synthesised and shown to undergo Diels–Alder cycloadditions exclusively from the carbonyl face. Steric environment seems to be predominantly responsible for the observed stereochemistry.

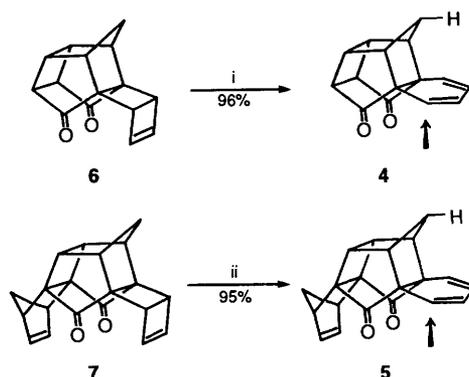
Stereoselectivity in [4 + 2]-cycloadditions to substrates embodying facially differentiated 1,3-diene moieties has attracted considerable attention in recent years and attempts have been made to evaluate critically the relative importance of steric, orbital and electrostatic effects in determining the π -face preferences.¹ In particular, diene units embedded within rigid polycyclic frames have proved to be valuable probes for diastereoselection with isodicyclopentadiene **1** standing out as a seminal example of such compounds.^{1a-d} More recently, cycloadditions to the polycyclic dienes **2** and **3**, wherein facial discrimination in the cyclohexadiene moiety is engendered through the steric effects of cyclobutyl hydrogens *vs.* the carbonyl orbital interactions (in **2**) and the steric effects of cyclobutyl hydrogens *vs.* the methano bridge hydrogen (in **3**), respectively, have been studied in detail.^{2,3} In **2**, the steric and orbital effects act cooperatively and carbonyl face selectivity is observed.² On the other hand, in **3** the relative steric environment directs cyclobutyl face selectivity.³ We thought that Diels–Alder cycloadditions to a related polycyclic diene **4** should nicely complement the earlier studies^{2,3} with **2** and **3**, since, in this case, the π -faces of the diene moiety are differentiated through the presence of the methano-bridge hydrogen and the carbonyl groups.



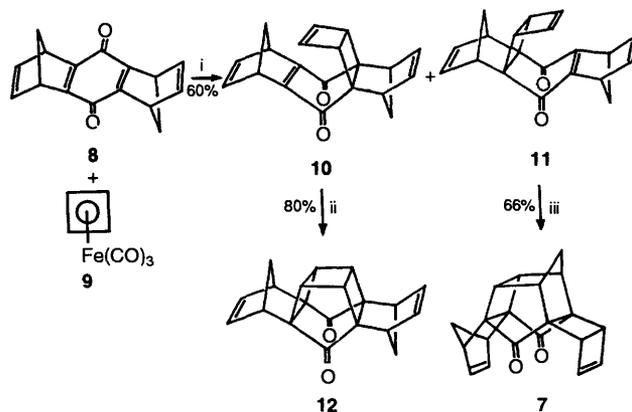
In this communication, we describe the synthesis of compound **4** and a closely related diene **5** and report on their [4 + 2]-cycloaddition stereoselectivities.

The two novel polycyclic dienes **4** and **5** were obtained in excellent yield through thermally induced cyclobutene ring opening in precursors **6** and **7**, respectively (see Scheme 1). We have previously reported the preparation of compound **6**⁴ and compound **7** was synthesised as outlined in Scheme 2. A Diels–Alder reaction between *anti*-bis-norbornobenzoquinone **8**⁵ and cyclobutadiene, liberated from its tricarbonyliron complex **9**, furnished two 1 : 1 adducts **10** and **11** (3 : 7) in 60% yield. Irradiation of the heptacyclic adducts **10** and **11** gave, by intramolecular [2 + 2]-cycloaddition, the nonacyclic diones **12** and **7**, respectively.

The three representative dienophiles, *viz.* maleic anhydride (MA), dimethylacetylene dicarboxylate (DMAD) and benzoquinone (BQ) underwent addition to compounds **4** and **5** when heated (110 °C) in toluene to furnish 1 : 1 adducts in near quantitative yield. Comparable conditions have been employed for cycloadditions to compounds **2** and **3** to furnish products



Scheme 1 Reagents and conditions: i, neat, 210 °C, 5 min; ii, neat, 220 °C, 5 min



Scheme 2 Reagents and conditions: i, CAN, acetone, 0 °C, 30 min; ii, hv, 450-W Hg lamp, Pyrex, EtOAc, 15 min; iii, hv, 450-W Hg lamp, Pyrex, EtOAc, 5 min

of kinetic control.^{2,3} The cycloadditions were monitored by TLC and the crude reaction mixture analysed by ¹H NMR spectroscopy. In each case, formation of only one adduct could be detected. Thus, compounds **4** and **5** furnished compounds **13** and **14** with MA, compounds **15** and **16** with DMAD and compounds **17** and **18** with BQ, respectively. The stereochemistry of the adducts **13**–**18** was established by analysis of the ¹H NMR data, particularly on the basis of the consistently large chemical-shift difference observed between the two protons of the methano group due to the field effect of the *syn* transannular double bond. Further, unambiguous proof of the stereochemistry of the adducts followed from the X-ray crystal structure determination of the **4** + MA adduct **13** (Fig. 1).

[4 + 2]-Cycloadditions to compounds **4** and **5** proceeded with overwhelming preference for the carbonyl face addition. It

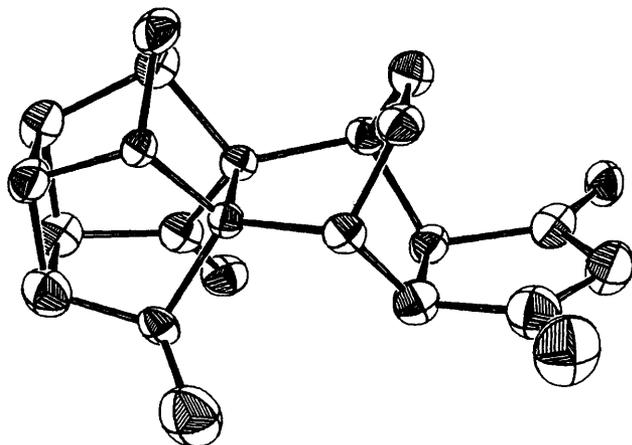
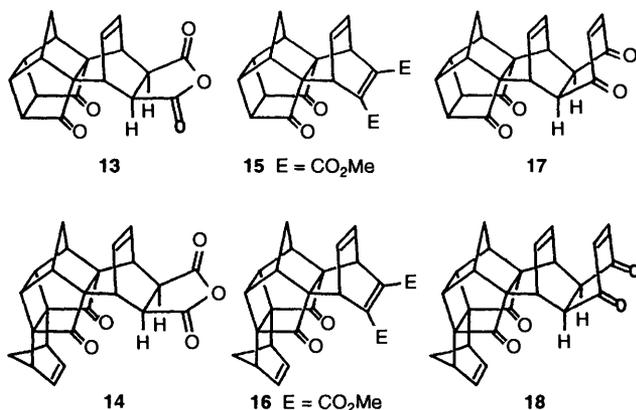


Fig. 1 ORTEP diagram of compound 13 (numbering scheme given will be the material deposited at the CCDC)



would appear that this selectivity originates solely on account of the greater nonbonded steric repulsions during dienophile capture on the methano face. However, in the light of the recent interpretation² of results with compound 2, concurrent benefit from secondary orbital effects for the addition from the carbonyl face of 4 and 5 remains a distinct possibility.

Experimental

All the compounds reported here were characterised on the basis of elemental analyses and spectroscopic data.

Hexacyclo[8.5.0.0^{3,8}.0^{3,14}.0^{8,12}.0^{11,15}]pentadeca-4,6-diene-2,9-dione 4 and *syn-Octacyclo*[8.5.4.1^{16,19}.0^{1,10}.0^{3,8}.0^{3,14}.0^{8,12}.0^{11,15}]eicosa-4,6,17-triene-2,9-dione 5.—The caged diones 6 and 7 (0.2 mmol) were each heated (neat) at 210–220 °C for 5 min under a nitrogen atmosphere. Each reaction mixture was then filtered through a silica gel (10 g) column, to furnish the dienes 4 and 5, respectively, which were recrystallised from dichloromethane–hexane. Compound 4: m.p. 164–166 °C; δ_{H} (CDCl₃, 100 MHz) 6.04–5.76 (2 H, m), 5.48–5.20 (2 H, m), 3.29–3.02 (2 H, m), 2.91 (2 H, m), 2.81–2.60 (2 H, m), 2.26 (1 H, 1/2 ABq, *J* 12), 1.90 (1 H, t of 1/2 ABq, *J*₁ 12, *J*₂ 1.5); δ_{C} (25.0

MHz) 211.31, 124.65, 121.83, 62.53, 54.06, 42.41, 39.06 and 38.82 (Found: C, 80.25; H, 5.4. C₁₅H₁₂O₂ requires C, 80.33; H, 5.39%). Compound 5: m.p. 244–246 °C; δ_{H} (CDCl₃, 200 MHz) 6.27 (2 H, br s with st, HC=CH), 6.00–5.85 (2 H, m), 5.46–5.32 (2 H, m), 2.91 (2 H, br s), 2.79 (4 H, s), 2.26 (1 H, 1/2 ABq, *J* 11.06), 1.98 (1 H, 1/2 ABq, *J* 11.18), 1.81 (1 H, 1/2 ABq, *J* 9.27), 1.60 (1 H, d of 1/2 ABq, *J*₁ 9.17, *J*₂ 1.5); δ_{C} (50 MHz) 211.20, 135.20, 124.30, 122.33, 62.53, 62.01, 53.73, 45.27, 42.22, 40.22 and 39.61 (Found: C, 83.5; H, 5.6. C₂₀H₁₆O₂ requires C, 83.31; H, 5.59%).

Crystal data for 13: C₁₉H₁₄O₅, *M*_r = 322.2, orthorhombic, *P*2₁2₁, *a* = 7.218(1) Å, *b* = 10.642(1) Å, *c* = 17.757(1) Å, *V* = 1363.99(2) Å³, *D*_x = 1.560 g cm⁻³, μ = 1.067 cm⁻¹, *F*(000) = 672, *Z* = 4. Intensity data were collected on an Enraf–Nonius CAD-4 automated diffractometer on a crystal of size 0.4 × 0.35 × 0.3 mm in the ω -2 θ scan mode. 1432 Reflections were measured out of which 1407 reflections were found to be unique and 1201 reflections were considered observed with *F*_o > 5.0 σ (*F*_o). Lorentz and polarisation corrections were applied. The structure was solved by direct methods using SHELXS 86.⁶ Full matrix least-squares refinement on *F*_o using SHELX 76⁷ with non-H atoms anisotropic and H atoms isotropic refinement converged to a final *R* factor of 0.035 and *R*_w = 0.039. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Acknowledgements

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