An Approach to Functionalized Cubanes. Regioselectivities and Frontier Molecular Orbital Analysis in the Addition of Dimethyl Cyclobutadiene-1,2-dicarboxylate to Quinones

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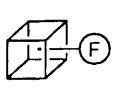
4 + 2 Cycloaddition between dimethyl cyclobutadiene-1,2-dicarboxylate and benzoquinone, **4**, gives **6**, **7** and **8** in the ratio 15:4:1. Similarly naphthoquinone, **5**, furnishes **9**, **10** and **11** in the ratio 11:1:2. Formation of symmetrical adducts is predominent in both cases. Irradiation of major adducts **6** and **9** results in a cascade of photorearrangements. Semiempirical AM1 calculations are used to rationalize the regioselectivities.

Highly functionalized cubane derivatives **1** have evoked a great deal of interest in recent years and have been projected as the promising materials for the 1990s and the 21st century.[1] Much of the efforts directed towards the synthesis of **1** have focused on the amplification of pre-existing functionality on the preformed cubane framework. In particular, placement of a polycarboxylic acid functionality has been considered advantageous and through innovative approaches a pentacarboxylated cubane **2** has been reported recently.[1,2]



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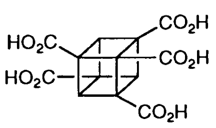

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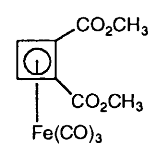

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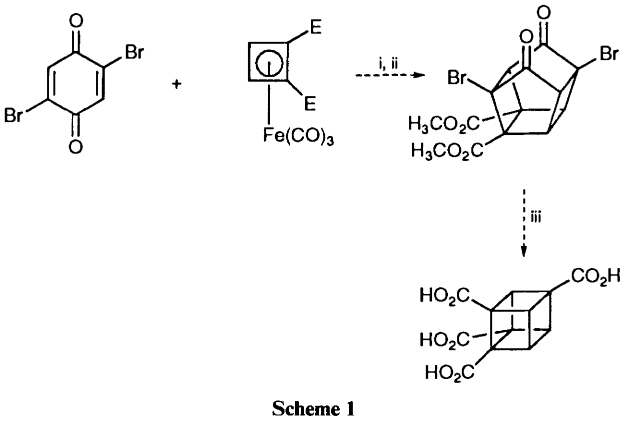
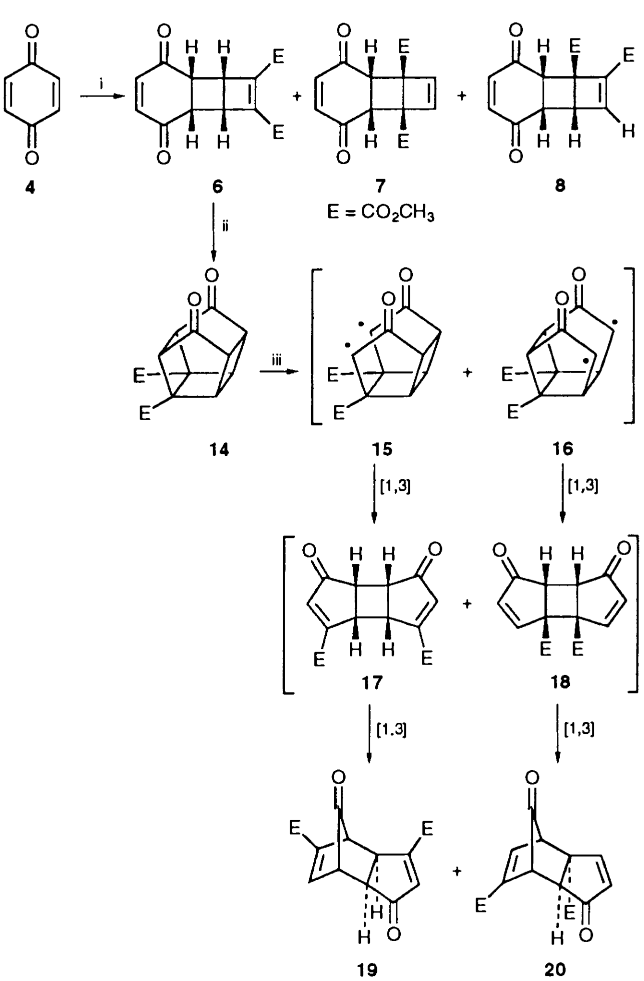
An alternative and simpler route to **1** might be possible by incorporating additional functionality into the precursors of cubane syntheses.[1a] This approach, within the framework of the Pettit cubane synthesis,[3] would require cycloaddition between a substituted benzoquinone and a functionalized cyclobutadiene, Scheme 1. Consequently, we have studied the cycloaddition between dimethyl cyclobutadiene-1,2-dicarboxylate liberated from the iron complex **3** and benzo- (**4**) and naphtho-quinones (**5**) and studied the photoirradiation of the derived major adducts. We have also performed semiempirical MO calculations to rationalize the regioselectivities in the cycloaddition between **3** and the quinones **4** and **5**.

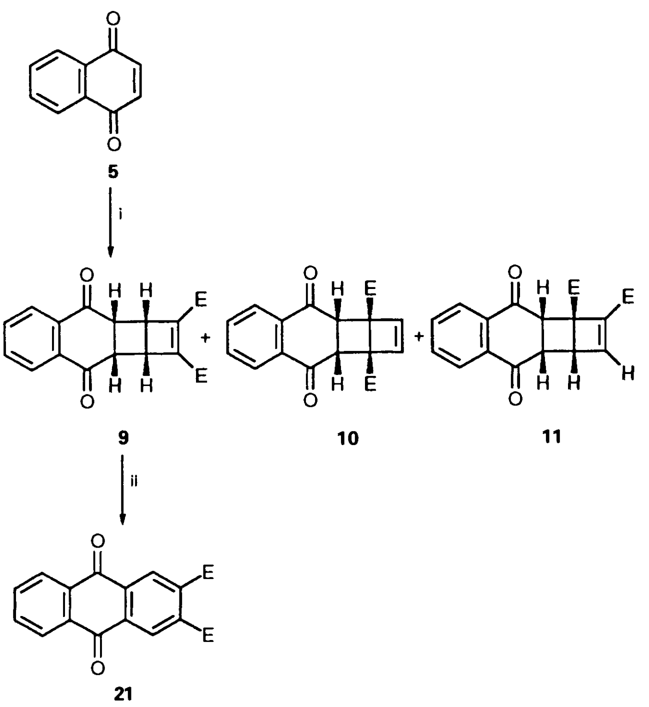


Scheme 1

Liberation of dimethyl cyclobutadiene-1,2-dicarboxylate from its iron tricarbonyl complex **3**[4,5] in the presence of benzoquinone **4** furnished three regioisomeric 1:1 adducts **6**, **7** and **8** in the ratio 16:4:1, respectively, in 40–50% yield. Structures of **6** and **7** were deduced on the basis of complementary ^{1}H and ^{13}C NMR data, while the presence of **8** was elicited from a chromatographically enriched fraction, Scheme 2. Similarly, disengagement of iron from **3** in the presence of naphthoquinone **5** yielded three regioisomeric adducts **9**, **10** and **11** in a 11:1:2 ratio, in over 80% yield. ^{1}H and ^{13}C data enable unambiguous structural assignment of all the three adducts, Scheme 3. The regioselectivities observed in the cycloaddition



Scheme 2 *Reagents:* i, **3**, CAN, 0 °C, acetone; ii, Pyrex, EtOAc; iii, *hν* (β-cleavage)



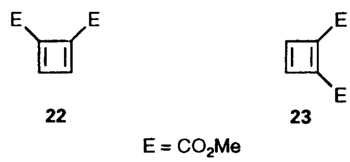
Scheme 3 *Reagents:* i, 3 CAN, 0 °C, acetone; ii, *hν*, EtOAc

to **4** and **5** have been further probed through MO calculations (*vide infra*).

As a prelude to the theme depicted in Scheme 1, photoirradiation of the major adducts **6** and **9** was studied. On irradiation with sunlight in a Pyrex vessel, **6** was seen to be consumed (TLC) and a complex mixture resulted, from which two strongly UV-absorbing products **19** and **20** (2:3) could be isolated in 30% yield. The structural identity of **19** and **20** was established through proton-decoupling experiments at 400 MHz. Formation of **19** and **20** was indicative of a cascade of photochemical reactions involving the pentacyclic cage dione **14**. Initial [2 + 2]-photocycloadditions in **6** furnished the intermediate **14**, which could not be purified owing to its propensity to form hydrates. Continued irradiation of **14** led to the intermediate tricyclic bis-enones **17** and **18** through an uncommon photochemical β-cleavage reaction followed by cyclobutane fragmentation.[6] Of **17** and **18**, the latter seems to predominate owing to preferred cleavage of the unsubstituted cyclobutane ring (broken lines in **14**). This preference can be understood in terms of the relative captodative stability of the two regioisomeric diradical intermediates, **15** and **16**, formed from **14** en route to **17** and **18**. While the acceptor groups flanking the diradical remain the same in **15** and **16**, the donor abilities of the cyclobutyl–carbinyl bond is clearly favoured in the latter.[7] The *cis*, *syn*, *cis*-tricyclic systems **17** and **18** undergo symmetry-allowed [1,3]-suprafacial shifts to furnish stereoselectivity *exo*-**19** and *exo*-**20**, respectively, as the end products of photoirradiation. There is precedence for the rearrangement of the type **17**→**19** and **18**→**20**.[8] While photolability of **14** thwarted further pursuit of Scheme 1, an interesting one-pot rearrangement sequence **6**→**14**→**17**→**19** has been observed.

The major adduct **9** from naphthoquinone on photoirradiation underwent only a cyclobutene ring-opening reaction and *in-situ* dehydrogenation to furnish the anthraquinonedicarboxylic acid diester **21** in 54% yield. The ^{1}H NMR spectral data of **19** enabled its ready characterization. No intramolecular cyclization products were detected in the case of **9**.

FMO Analysis.—1,2-Disubstituted cyclobutadienes released from Fe(CO)$_3$ exists in two isomeric forms **22** and **23** which are



in dynamic equilibrium.[9] We have studied the frontier orbital control of dimethyl cyclobutadiene-1,2-dicarboxylate–quinone cycloadditions using the semiempirical AM1 Method.[10] Calculations indicate that **22** is more stable than **23** by 1.1 kcal mol^{-1}.†‡ The frontier orbitals, HOMO and LUMO, of the two forms of the cyclobutadienes are depicted in Fig. 1. These are very similar. The difference in the coefficient sizes on all the carbons is extremely small and should contribute little to the regioselectivity.

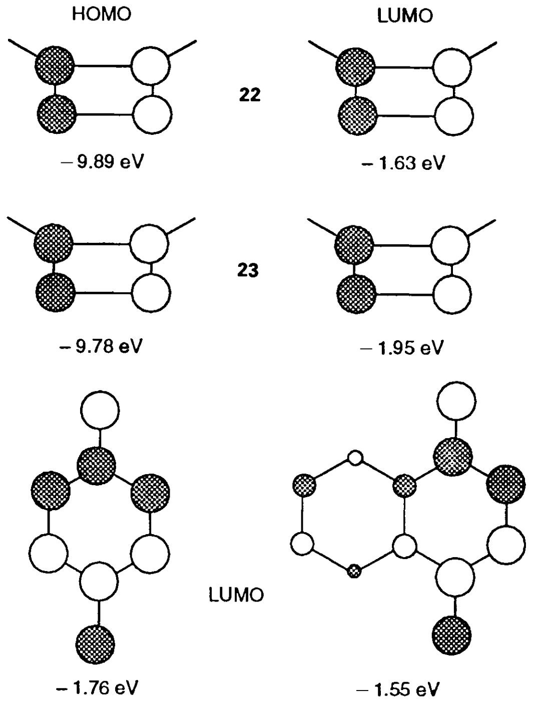


Fig. 1 Frontier orbitals of the cyclobutadiene **22** and **23**

The benzoquinone HOMO is a π MO based on the benzene ring with no coefficient on the quinone double bond and hence can have little intereaction with the cyclobutadiene molecule. The LUMO is a π* of the quinone double bond and suitable to interact with the cyclobutadiene molecule. The energy difference [HOMO (of **22**) − LUMO (of **4**)] is 8.13 eV. The HOMO + 1 of **4** has the right symmetry to interact but the energy difference (LUMO − HOMO + 1 = 9.64 eV) is very large. Similarly, in naphthoquinone only the LUMO has the appropriate symmetry to interact with the cyclobutadiene orbitals, HOMO (of **22**) − LUMO (of **5**) is 8.34 eV. The HOMO of naphthoquinone does not have the right symmetry. HOMO + 3, the orbital with the right symmetry, is not energetically favourable (LUMO of **22** − HOMO + 3 of **5** = 9.57 eV). Fig. 1 gives the LUMOs of benzoquinone and naphthoquinone which have the right symmetry to interact with

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† Such small energy differences are expected in these systems. The corresponding difference for the dicyano derivative is calculated to be 0.85 kcal mol^{-1} at the AM1 and 2.47 kcal mol^{-1} at the HF/6-31G* level. Semiempirical studies of vicinal diphenylcyclobutadienes has given a difference of about 1 kcal mol^{-1} between the two isomers.[11]

‡ 1 cal = 4.184 J.

the cyclobutadiene orbitals. The adduct formation is essentially controlled by the interaction between the LUMO of quinone and the HOMO of cyclobutadiene. On [4 + 2]-cycloaddition with quinones, **22** gives rise to symmetrical adducts and **23** gives unsymmetrical adducts. As **22** is more stable than **23** by 1.1 kcal mol^{-1}, **22** is present in excess at equilibrium. This may explain the preferential formation of symmetric products (**6**, **7** and **9**, **10**) compared with the unsymmetrical products (**8** and **11**). All the cycloadditions benefit from the secondary orbital interactions roughly to the same extent.[12]

We are not able to give a clear explanation for the ratio of the symmetrical adducts obtained. Molecular mechanics calculations show that the transition states for the formation of **6** and **9** are sterically less favoured than those corresponding to **7** and **10** by *ca.* 4 kcal mol^{-1}. AM1 calculations indicate that **6** and **9** are more stable than **7** and **10** by 12.2 and 11.8 kcal mol^{-1}, respectively. In the absence of any clear preference based on FMO theory, we attribute the results to the greater stability of **6** and **9**. This is also supported by our previous results on the oligomerization of dimethyl cyclobutadiene-1,2-dicarboxylate and its cycloaddition with norbornadiene.[13,14]

Experimental

Diels–Alder Reaction between p-*Benzoquinone and Dimethyl Cyclobutadiene*-1,2-*dicarboxylate*.—A solution of *p*-benzoquinone (70 mg, 0.64 mmol) and dimethyl cyclobutadiene-1,2-dicarboxylate–iron tricarbonyl complex **3** (200 mg, 0.64 mmol) in dry acetone (5 cm^3) was cooled to 0 °C. Ceric ammonium nitrate (1.071 g, 1.94 mmol) was slowly added to this solution in portions and the stirring was continued for 4 h. The reaction mixture was quenched with water (5 cm^3) and extracted with dichloromethane (3 × 15 cm^3). Removal of the solvent at room temperature under reduced pressure gave a crude mixture (174 mg). The ^{1}H NMR spectrum of this mixture indicated the presence of adducts **6**, **7** and **8** in the ratio 15:4:1. On fractional crystallization from dichloromethane–hexane the major adduct **6** (57 mg, 32%) was readily obtained: m.p. 118–119 °C; ν_{max}(KBr)/cm^{-1} 2950, 1720, 1630 and 1600; δ_H(CDCl$_3$; 100 MHz) 6.7 (2 H, s, –CO–CH=CH–CO), 3.86 (4 H, m) and 3.76 (6 H, s, CO$_2$CH$_3$); δ_C(CDCl$_3$; 25.0 MHz) 195.71, 160.30, 143.95, 143.47, 52.12, 43.00 and 41.47 (Found: C, 60.6; H, 4.3. $C_{14}H_{12}O_6$ requires C, 60.87; H, 4.38%). The mother liquor, after separation of **6**, was concentrated and chromatographed on a silica gel column. Elution with 40% ethyl acetate–hexane furnished the minor adduct **7** (23 mg, 12.8%): m.p. 85–86 °C; ν_{max}(KBr)/cm^{-1} 2950, 1720, 1680 and 1600; δ_H(CDCl$_3$; 100 MHz) 6.78 (2 H, s, –CO–CH=CH–CO–), 6.36 (2 H, s, –CH=CH–), 4.16 (2 H, s, –COC*H*–) and 3.76 (6 H, s, CO$_2$C*H*$_3$); δ_C(CDCl$_3$; 25.0 MHz) 195.47, 168.59, 143.83, 138.83, 59.59, 52.94 and 42.94 (Found: C, 60.8; H, 4.35. $C_{14}H_{12}O_6$ requires C, 60.87; H, 4.38%). The overall recovery was only 45% and it would seem that considerable decomposition had occurred on the column.

Diels–Alder Reaction between 1,4-*Naphthoquinone and Dimethyl Cyclobatadiene*-1,2-*dicarboxylate*.—A solution of 1,4-naphthoquinone (130 mg, 0.82 mmol) and dimethyl cyclobutadiene-1,2-dicarboxylate–iron tricarbonyl complex **3** (253 mg, 0.82 mmol) in dry acetone (10 cm^3) was cooled to 0 °C. Ceric ammonium nitrate (1.35 g, 2.46 mmol) was slowly added in portions and stirring was continued for 5 h after which the reaction mixture was quenched with water (5 cm^3) and extracted with dichloromethane (3 × 15 cm^3) removal of the solvent at room temperature under reduced pressure gave a crude mixture (275 mg) which was loaded onto a silica gel column. Elution with 30% ethyl acetate–hexane gave the minor adduct **11** (18 mg, 6.7%) which was recrystallized from dichloromethane–hexane: m.p. 118–119 °C; ν_{max}(KBr)/cm^{-1} 2970, 1725, 1680 and 1595; δ_H(CDCl$_3$; 100 MHz) 7.9 (4 H, m), 6.34 (2 H, s, –C*H*=C*H*–), 4.38 (2 H, s, COCH) and 3.81 (6 H, s, CO$_2$CH$_3$); δ_C(CDCl$_3$; 25.0 MHz) 194.20, 168.88, 139.00, 136.95, 134.71, 127.42, 59.47, 52.88 and 44.12 (Found: C, 66.45; H, 4.3. $C_{18}H_{14}O_6$ requires C, 66.25; H, 4.32%). Further elution of the column with the same eluent gave the adduct **10** (30 mg, 11.2%) which was recrystallized from dichloromethane–hexane: m.p. 155–156 °C; ν_{max}(KBr)/cm^{-1} 2950, 1730, 1710, 1675 and 1600; δ_H(CDCl$_3$; 100 MHz) 7.87 (4 H, m), 6.86 (1 H, s), 4.48 (1 H, m), 3.98 (2 H, m), 3.82 (3 H, s, CO$_2$CH$_3$) and 3.65 (3 H, s, CO$_2$C*H*$_3$); δ_C(CDCl$_3$; 25.0 MHz) 195.24, 192.95, 169.42, 147.42, 139.54, 136.83, 134.71, 134.48, 127.47, 127.12, 55.65, 52.82, 51.70, 46.47, 42.88 and 42.53 (Found: C, 66.3; H, 4.25. $C_{18}H_{14}O_6$ requires C, 66.25; H, 4.32%). Continued elution with 40% ethyl acetate–hexane gave the major adduct **9** (196 mg, 73%) and was recrystallized from dichloromethane–hexane: m.p. 119–120 °C; ν_{max}(KBr)/cm^{-1} 2950, 1735, 1710, 1675 and 1600; δ_H(CDCl$_3$; 100 MHz) 7.27 (4 H, m, ArH), 3.98 (4 H, d, *J* = 3 Hz) and 3.61 (6 H, s, CO$_2$CH$_3$); δ_C(CDCl$_3$; 25.0 MHz), 194.30, 160.06, 143.67, 137.12, 134.36, 127.06, 51.88, 43.06, 42.59 (Found: C, 66.3; H, 4.4. $C_{18}H_{14}O_6$ requires C, 66.25; H, 4.32%). The combined yield of **9**–**11** was 91% in the ratio 11:1:2.

Sunlight Irradiation of the Adduct **6**.—A solution of the adduct **6** (50 mg, 0.18 mmol) in 90 cm^3 of ethyl acetate was irradiated in a Pyrex vessel with sunlight for 3–4 h. After concentration under reduced pressure the residue was loaded onto a silica gel column and elution with 40% ethyl acetate-hexane furnished a mixture of the tricyclic enones **19** and **20** (15 mg, 30%) in a 2:3 ratio (by ^{1}H NMR spectroscopy). δ_H(CDCl$_3$; 400 MHz) 7.55 (1 H, d, *J* = 8 Hz, C5-H in **20**), 7.52 (1 H, d, *J* = 4 Hz, C9-H in **19**), 7.42 (1 H, d, *J* = 3.2 Hz, C8-H in **20**), 6.82 (1 H, br s, C4-H in **19**), 6.30 (1 H, d, *J* = 4 Hz, C4-H in **20**), 3.90 (3 H, s, CO$_2$CH$_3$), 3.82 (3 H, s, CO$_2$CH$_3$), 3.80 (3 H, s, CO$_2$CH$_3$), 3.74 (3 H, s, CO$_2$C*H*$_3$), 3.64 (1 H, br s, C1-H in **20**), 3.6–3.5 (1 H, m, C7-H in **20**), 3.48 (1 H, d, *J* = 4 Hz, C1-H in **19**), 3.31 (1 H, d, *J* = 8 Hz, C2-H in **19**), 2.93 (1 H, s, C2-H in **20**) 2.70 (1 H, d, *J* = 8 Hz, C6-H in **19**); ν_{max}(neat)/cm^{-1} 2950, 1790, 1710, 1690 and 730.

Irradiation of the Adduct **9**.—A solution of the adduct **9** (15 mg, 0.046 mmol) in 125 cm^3 of ethyl acetate was irradiated using a 450 W Hanovia Hg lamp with a Pyrex filter for 6 min. The solvent was removed and the residue was loaded onto a silica gel column. Elution with 40% ethyl acetate–hexane furnished the anthraquinone diester **21** (8 mg, 54%) and was recrystallized from dichloromethane–hexane: m.p. 158–160 °C (lit.,[15] m.p. 160 °C); ν_{max}(KBr)/cm^{-1} 2950, 1730, 1680 and 1600; δ_H(CDCl$_3$; 100 MHz) 8.69 (2 H, s), 8.08 (4 H, m), 4.0 (6 H, s, CO$_2$CH$_3$) (Found: C, 67.0; H, 3.7. $C_{18}H_{12}O_6$ requires C, 66.67; H, 3.73%).

Acknowledgements

M. B. V. and G. N. S. thank the Council of Scientific and Industrial Research, New Delhi for Senior Research Fellowships. We also thank a referee for a helpful suggestion.

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Paper 3/05521C
Received 14*th September* 1993
Accepted 3rd *December* 1993