Cycloaddition between 2,3-Dibromo-5,6-trinorbornenobenzoquinone and 1,2-Bis(methoxycarbonyl)cyclobutadiene: Intervention of a Fragmentation Reaction during Quest for Annulated, Functionalized Cubanes

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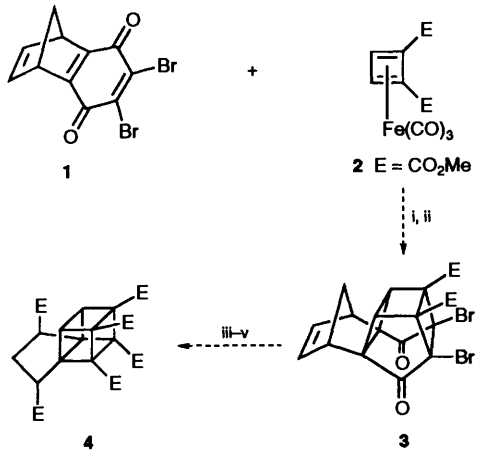
Diels–Alder reaction between 1,2-bis(methoxycarbonyl)cyclobutadiene **2** and quinone **1** predominantly furnished adduct **5**, which on photolysis gave the annulated secopentaprismane dione **3**. Attempted double-ring-contraction on compound **3** took a devious course to furnish a fragmentation product **11** *via* tandem Haller–Bauer cleavage and fragmentation.

The past decade has been witness to a renaissance in cubane chemistry.[1] This surge can be attributed to the initial promising observations and further predictions that cubane derivatives can serve as remarkably versatile advanced materials.[1b] Indeed, uses ranging from powerful explosives and propellants to antiviral agents to liquid crystalline materials have been projected for a variety of cubane derivatives. These promising leads naturally require convenient access to cubane derivatives with diverse and extensive functionalization. The two landmark syntheses[2] of cubanes and their modifications,[2c,d] though elegant in concept, provide cubane derivatives with only limited functionalization. Recent efforts have, therefore, focused on the amplification of functionality on the preformed cubane core and some success has been achieved.[1,3]

We reasoned that an alternative way to access highly functionalized cubanes would be through the deployment of more functionally embellished starting materials within the Eaton[2a] or Pettit[2b] cubane syntheses.[4] In our assessment, the Pettit synthesis appeared to be more suited for this strategy. Consequently, we selected 2,3-dibromo-5,6-trinorbornenobenzoquinone **1**[5] and 1,2-bis(methoxycarbonyl)cyclobutadiene **2**[6] as the starting materials and hoped to find a way to produce annulated and densely functionalized cubane derivative **4** through the intermediate caged dione **3** as depicted in Scheme 1.[7] However, the pursuit of this theme in actuality led to a more eventful but less desirable outcome and our observations are recorded in this report.



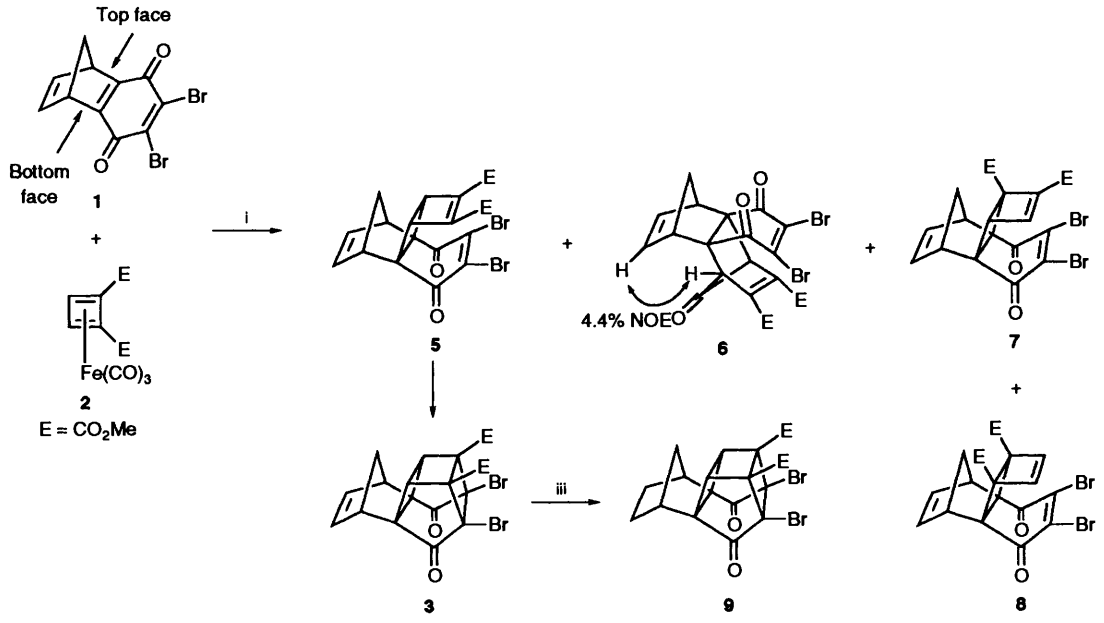
Scheme 1 *Reagents and conditions:* i, Ce^{4+}; ii, *hν*; iii, OH^-; iv, [O]; v, CH_2N_2

Results and Discussion

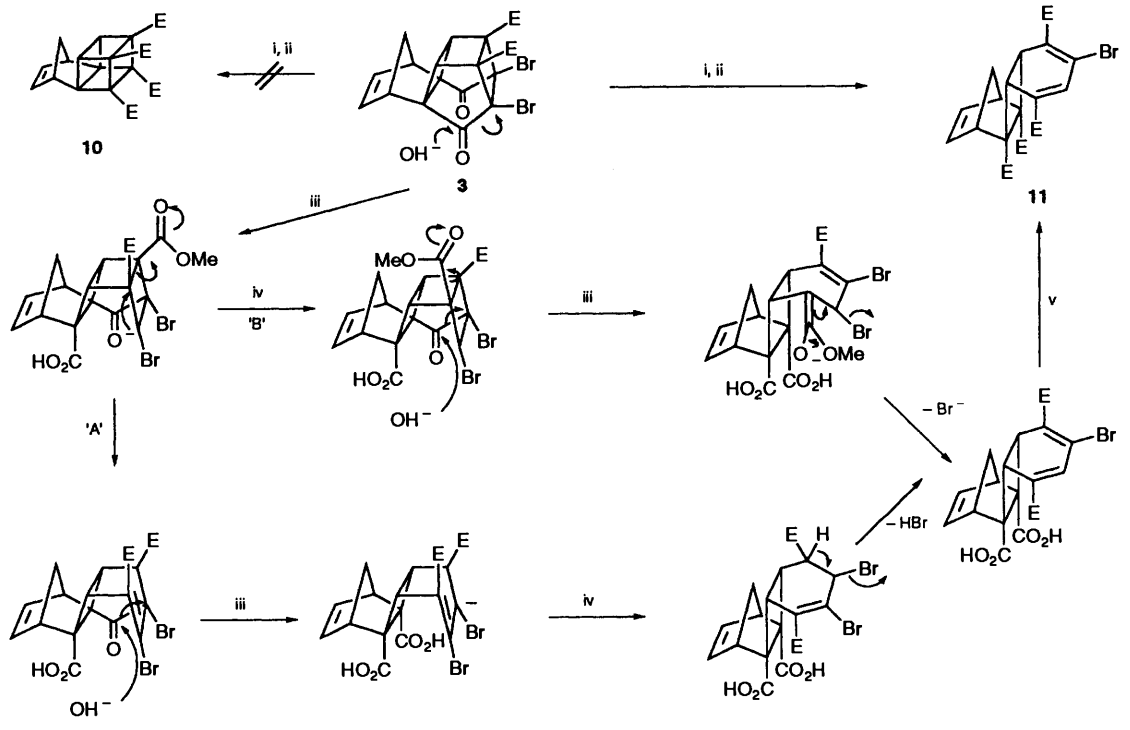
Reaction between quinone **1** and cyclobutadiene diester, disengaged from complex **2**, furnished four 1:1 Diels–Alder addition products **5**, **6**, **7** and **8** (41:3:1:1) in 92% yield, Scheme 2. There was high selectivity for and preponderance of the adduct **5**. The ^1H NMR spectra of the adducts **5–8** clearly indicated that they are all derived through addition to the central bond of the quinone **1** as the deshielded trinorbornadiene olefinic protons ($\delta \sim 6.86$) in quinone **1** had shifted to δ 6.1–6.5 in the adducts. Owing to the presence of bromine substitution on the terminal quinone double bond, products corresponding to addition at peripheral positions were not observed. The stereochemistry of compounds **5**, **7** and **8**, indicating preferred addition on the top face of the quinone moiety, was deduced from the subtle and internally consistent shielding of the trinorbornene olefinic protons (δ 6.15 in **5**, 6.17 and 6.20 in **7** and 6.17 in **8**) by the distal quinone double bond due to the folded topology of these adducts.[7] The unusual structure **6** formed through insertion of CO was recognized on the basis of its mass spectral data, nuclear Overhauser effect (NOE) study and carbonyl absorption in the IR spectrum at $\sim 1750\ cm^{-1}$ due to the trinorbornen-7-one moiety.

Irradiation of triene **5** through a Pyrex filter led to the heptacyclic dione diester **3** in good yield. Absence of tetrasubstituted olefinic carbons in the ^{13}C NMR spectrum, and shift in the carbonyl absorption (ν 1695 to 1775 cm^{-1}) were firm indications that the desired intramolecular [2 + 2]cyclization had occurred. On catalytic hydrogenation, alkene **3** furnished saturated ring system **9** whose ^1H and ^{13}C NMR data further reinforced their formulation.

The annulated dibromosecopentaprismane dione diester **3** with two-fold symmetry was assembled in order to effect a two-fold Favorskii-type ring contraction to give the functionalized propellacubane derivatives like **4** and **10**. Thus, dione **3** was treated with aq. methanolic KOH and the crude product was esterified with diazomethane. The resulting product, a tetra-ester, turned out to have unexpected structure **11** arising through fragmentation rather than the desired tetra ester **10**. Several variations in the reaction conditions for the Favorskii rearrangement did not help in producing the hoped for cubane **10**. The structure of product **11**, totally devoid of symmetry, was based on the appearance of 6 sp^2 olefinic carbons (^{13}C NMR), the presence of conjugation (UV), loss of one bromine [low-resolution mass spectroscopy (LRMS)] and the presence of a deshielded β-proton (δ 6.96) of an α,β-unsaturated ester moiety. A plausible mechanism for the formation of compound **11** is shown in Scheme 3. However, it is not clear whether the fragmentation step precedes (path 'A') or follows (path 'B') the



Scheme 2 *Reagents and conditions:* i, Ce^{4+}, 0 °C, 1 h (92%); ii, *hv*, Pyrex filter, EtOAc, 15 min (83%); iii H_2/Pd–C, EtOAc, 1 h (100%)



Scheme 3 *Reagents:* i, aq. KOH, MeOH; ii, CH_2N_2, Et_2O; iii, OH^-; iv, water; v, CH_2N_2

second Haller–Bauer cleavage.[8] Thus, while we could readily assemble the precursor **3**, intervention of the strain-releasing Haller–Bauer cleavage in preference to the Favorskii ring contraction, and subsequent fragmentation, thwarted our attempts to access our target compounds **4** or **10**.[9]

Experimental

NMR spectra were recorded in $CDCl_3$ solvent with $SiMe_4$ as internal standard on a JEOL FX-100 and Bruker 200 spectrometers. ^1H NMR spectra were recorded at 100 MHz and ^{13}C NMR spectra were recorded at 25.0 MHz, unless otherwise mentioned. *J* Values are given in Hz. IR spectra were recorded on a Perkin–Elmer model 1310 spectrometer.

Diels–Alder Reaction between 2,3-Dibromotrinorbornenobenzoquinone **1** *and 1,2-Bis(methoxycarbonyl)cyclobutadiene.*—A solution of the 2,3-dibromotrinorbornenobenzoquinone **1** (268 mg, 0.812 mmol) and 1,2-bis(methoxycarbonyl)cyclobutadiene–iron tricarbonyl complex **2** (250 mg, 0.812 mmol) in dry acetone (25 cm^3) was cooled to 0 °C. Solid cerium(IV) ammonium nitrate was added portionwise to the stirred mixture until evolution of gases ceased. The mixture was stirred for an additional 10 min. Acetone was removed under reduced pressure at room temperature and the residue was diluted with water (20 cm^3) and extracted with dichloromethane (3 × 50 cm^3). Removal of the solvent gave a mixture of adducts, which was charged on a silica gel (50 g) column. Elution with 10% ethyl acetate–hexane gave syn, endo-*dimethyl* 12,13-*dibromo*-11,14-*dioxopentacyclo*[4.4.4.$1^{2,5}$.$0^{1,6}$.$0^{7,10}$]*pentadeca*-3,8,12-*triene*-7,10-*dicarboxylate* **8** (8 mg, 2%), which was recrystallized from dichloromethane–hexane, m.p. 168–169 °C; ν_{max}(KBr)-

cm^{-1} 2950, 1730, 1690, 1270, 725 and 690; δ_H 6.32 (2 H, s, cyclobutenyl HC=CH), 6.17 (2 H, br s with st, trinorbornenyl HC=CH), 3.80 (6 H, s, CO_2Me), 3.74 (2 H, br s with st, C*H*–CH=CH), 2.27 (1 H, 1/2 ABq, *J* 11) and 1.77 (1 H, 1/2 ABq, *J* 11) (Found: C, 46.0; H, 2.85. $C_{19}H_{14}Br_2O_6$ requires C, 45.80; H, 2.83%). Further elution of the column with the same eluent furnished the syn, endo-dimethyl 12,13-*dibromo*-11,14-*dioxopentacyclo*[4.4.4.$1^{2,5}$.$0^{1,6}$.$0^{7,10}$]*pentadeca*-3,8,12-*triene*-7,8-*dicarboxylate* **7** (8 mg, 2%), which was recrystallized to furnish bright yellow crystals, m.p. 184 °C; ν_{max}(KBr)/cm^{-1} 2960, 1740, 1720, 1690, 1600, 1230 and 690; δ_H(500 MHz) 6.92 (1 H, s, *H*C=CCO$_2$Me), 6.20 (1 H, d of 1/2 ABq, J_1 5.5, J_2 3, *H*C=CH–), 6.17 (1 H, d of 1/2 ABq, J_1 5.5, J_2 3, HC=C*H*), 3.91 (1 H, br s with st), 3.81 (3 H, s, CO_2Me), 3.72 (3 H, s, CO_2Me), 3.60 (1 H, s), 3.42 (1 H, br s with st), 1.83 (1 H, 1/2 ABq, *J* 10.4) and 1.69 (1 H, 1/2 ABq, *J* 10.4 (Found: C, 45.85; H, 2.8%).

Continued elution of the column using the same solvent mixture gave the adduct dimethyl 12,13-dibromo-11,14,15-trioxopentacyclo[4.4.4.$1^{2,5}$.$1^{7,10}$.$0^{1,6}$]hexadeca-3,8,12-triene-3,4-dicarboxylate **6** (24 mg, 6%), which was recrystallized from dichloromethane–hexane to furnish bright yellow crystals, m.p. 177–178 °C; ν_{max}(KBr)/cm^{-1} 2950, 1750, 1720, 1680, 1635, 745 and 730; δ_H(500 MHz) 6.51 (2 H, dd, $J_1 = J_2 = 2$, HC=CH), 3.78 (6 H, s, CO_2Me), 3.56 (2 H, dd, $J_1 = J_2 = 2$, C*H*CH=CH), 3.36 (2 H, s, C*H*C=C), 1.78 (1 H, 1/2 ABq, *J* 9.6) and 1.32 (1 H, 1/2 ABq, *J* 9.6) [Found: 527 ($M^+ + 1$). $C_{20}H_{14}Br_2O_7$ requires *M*, 526].

Lastly, continued elution with 20% ethyl acetate-hexane furnished the syn,endo-*dimethyl*-12,13-*dibromo*-11,14-*dioxopentacyclo*-[4.4.4.$1^{2,5}$.$0^{1,6}$.$0^{7,10}$]*pentadeca*-3,8,12-*triene*-8,9-*dicarboxylate* **5** (335 mg, 82%), which was recrystallized from dichloromethane–hexane to furnish beautiful, bright yellow crystals, m.p. 208–209 °C; ν_{max}(KBr)/cm^{-1} 2980, 1715, 1692, 1630, 1295 and 690; δ_H 6.15 (2 H, br s with st, HC=CH), 3.77 (6 H, s, CO_2Me), 3.57 (2 H, s, C*H*C=C), 3.48 (2 H, br s with st, CHCH=CH), 2.08 (1 H, 1/2 ABq, *J* 10) and 1.68 (1 H, 1/2 ABq, *J* 10); δ_C 187.84, 164.18, 149.12, 142.65, 139.24, 59.29, 52.35, 48.88, 46.41 and 41.83 (Found: C, 45.7; H, 2.8. $C_{19}H_{14}Br_2O_6$ requires C, 45.80; H, 2.83%).

syn-*Dimethyl*-4,9-*Dibromo*-3,10-*dioxoheptacyclo*[10.2.1.$0^{2,6}$.$0^{2,11}$.$0^{4,9}$.$0^{5,8}$.$0^{7,11}$]*pentadeca*-13-*ene*-5,8-*dicarboxylate* **3**.—A solution of the enedione **5** (60 mg, 0.12 mmol) in ethyl acetate (125 cm^3) was irradiated with a 450 W Hg lamp in a quartz vessel using a Pyrex filter for 20 min. Solvent was removed and the residue was charged on a silica gel (20 g) column. Elution with 40% ethyl acetate–hexane furnished the dibromoheptacyclic dione diester **3** (50 mg, 83%), which was recrystallized from dichloromethane–hexane, m.p. 171–172 °C; ν_{max}(KBr)/cm^{-1} 2950, 1755, 1730, 1435, 1320 and 730; δ_H 6.36 (2 H, br s, HC=CH), 3.81 (6 H, s, CO_2Me), 3.62 (2 H, s, cyclobutyl CH), 3.18 (2 H, br s, C*H*CH=CH) and 2.04–1.48 (2 H, m, CH_2); δ_C 198.24, 166.06, 135.06, 69.29, 63.71, 56.47, 52.71, 45.59, 43.53 and 40.59 (Found: C, 45.75; H, 2.8. $C_{19}H_{14}Br_2O_6$ requires C, 45.80; H, 2.83%).

syn-*Dimethyl*-4,9-*Dibromo*-3,10-*dioxoheptacyclo*[10.2.1.$0^{2,6}$.$0^{2,11}$.$0^{4,9}$.$0^{5,8}$.$0^{7,11}$]*pentadecane*-5,8-*dicarboxylate* **9**—A solution of the heptacyclic dione **3** (30 mg, 0.06 mmol) in ethyl acetate (5 cm^3) was hydrogenated over 5% Pd/C catalyst. The catalyst was filtered off and the residue was filtered through a silica gel (10 g) column. Elution with 25% ethyl acetate–hexane furnished the perhydro compound **9** (30 mg, 100%), which was recrystallized from dichloromethane–hexane, m.p. 169–170 °C; ν_{max}(KBr)/cm^{-1} 2950, 1755, 1710, 1440, 1335 and 1305; δ_H 3.79 (6 H, s, CO_2Me), 3.58 (2 H, s, cyclobutyl CH), 2.64 (2 H, m, bridgehead C*H*) and 2.24–1.35 (6 H, series of m); δ_C (50 MHz) 198.92, 166.13, 70.34, 58.18, 56.23, 52.56, 52.37, 41.87, 38.54 and 21.72 (Found: C, 45.7; H, 3.25. $C_{19}H_{16}Br_2O_6$ requires C, 45.62; H, 3.22%).

exo,anti,cis-*Tetramethyl* 5-*Bromotetracyclo*[8.2.1.$0^{2,9}$.$0^{3,8}$]-*trideca*-4,6,11-*triene*-2,4,7,9-*tetracarboxylate* **11**.—To a solution of the caged dione **3** (75 mg, 0.151 mmol) in methanol (8 cm^3) were added KOH (200 mg) and water (2 cm^3). The mixture was stirred at room temperature for 14 h. Methanol was removed under reduced pressure, and the residue was diluted with water (5 cm^3) and acidified to pH ~ 4 with dil. HCl. The acidified solution was extracted with ethyl acetate (3 × 25 cm^3) and the combined extracts were washed with water and dried. Removal of the solvent gave a crude material, which was dissolved in methanol (1 cm^3) and esterified with an ethereal solution of diazomethane at 0 °C. The solvent was evaporated off and the residue was charged on a silica gel (10 g) column. Elution with 15% ethyl acetate–hexane gave tetraester **11** (24 mg, 33%), which was recrystallized from dichloromethane–hexane, m.p. 146–147 °C; λ_{max}(MeOH)/nm 328.6 and 313.1 (fine structure); ν_{max}(KBr)/cm^{-1} 2950, 1730, 1435, 1255 and 1105; δ_H 6.96 (1 H, s, *H*C=C–CO_2Me), 6.09 (2 H, br s, HC=CH), 3.77 (3 H, s, CO_2Me), 3.75 (3 H, s, CO_2Me), 3.52 (2 H, s), 3.51 (3 H, s, CO_2Me), 3.49 (3 H, s, CO_2Me), 3.09 (2 H, br s, C*H*CH=CH), 1.95 (1 H, 1/2 ABq, *J* 10) and 1.63 (1 H, 1/2 ABq, *J* 10); δ_C 170.77, 170.30, 166.18, 165.59, 135.89, 135.47, 135.18, 131.59, 127.59, 122.71, 65.94, 64.29, 52.12, 51.82, 51.65, 51.35, 49.29, 49.00, 44.00, 40.88 and 36.64 (Found: C, 52.3; H, 4.4%; M^+, 481. $C_{21}H_{21}BrO_8$ requires C, 52.40; H, 4.39%; *M*, 481).

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