

Ring-expansion of Carbocyclic β -Ketoesters with Acetylenic Esters

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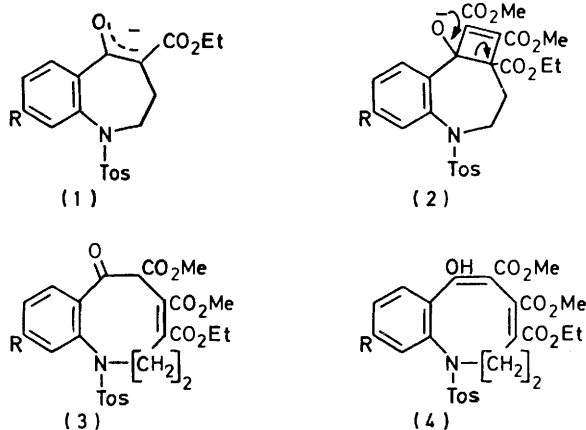
Sodium salts of 2-methoxycarbonyl-cyclopentanone, -cyclohexanone, -cycloheptanone, -cyclo-octanone and -cyclododecanone react with dimethyl acetylenedicarboxylate to yield, after neutralisation, 1-hydroxy-2,3,4-trismethoxycarbonyl-cyclohepta-, -cyclo-octa-, -cyclonona-, -cyclodeca-, and -cyclotetra-deca-1,3-diene, respectively. In a similar fashion 2-methoxycarbonylcyclopentanone gave 9-hydroxy-6,7,8-trismethoxycarbonyl-5*H*-benzocycloheptene while methyl 1,2,3,4-tetrahydro-1-oxonaphthalene-2-carboxylate and 6,7,8,9-tetrahydro-6-methoxycarbonylbenzocyclohepten-5-one gave respectively the corresponding eight- and nine-membered ring compounds. Methyl propiolate was shown to participate in analogous reactions with 2-methoxycarbonylcyclopentanone, methyl 1,2,3,4-tetrahydro-1-oxonaphthalene-2-carboxylate, and methyl 1,2,3,4-tetrahydro-6-methoxy-1-oxonaphthalene-2-carboxylate. In the latter case a low yield of 9,10-dihydro-2-methoxy-6,7,8-trismethoxycarbonyl-6*H*-benzocyclo-octen-5-one was accompanied by the isomeric Michael adduct. Some reactions of the ring-expanded products are described.

IN 1974¹ we reported that the anion (1; R = H) reacted with dimethyl acetylenedicarboxylate yielding a 1:1 adduct which still contained the enolisable β -ketoester chromophore. It was supposed that reaction had proceeded *via* (2; R = H) to give the 1-benzazonine (3;

N.m.r. spectroscopy (see Experimental section) lent further support; in particular an enolic carbonyl at δ 181.9 along with *one* signal at δ 98.5 (C-2 of ring) favours structure (6, $n = 3$) and excludes structure (7).

Secondly, higher homologues (5; $n = 4, 5, 6$, and 10) were subjected to similar treatment and in each case enolic compounds (6; $n = 4, 5, 6$, and 10) were obtained in about 50% yield. Their structures were determined as for the case above (6; $n = 3$). The products show the chemical properties expected for β -keto-esters; thus acid hydrolysis of the product (6; $n = 4$) gave the keto-anhydride (10) in good yield while products (6; $n = 3-6$) reacted with phenylhydrazine to provide the pyrazolones (11; $n = 3-6$) in acceptable yields.

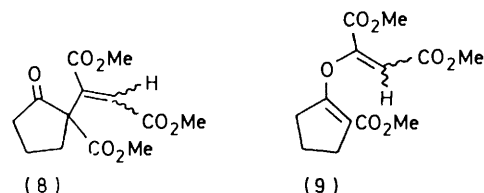
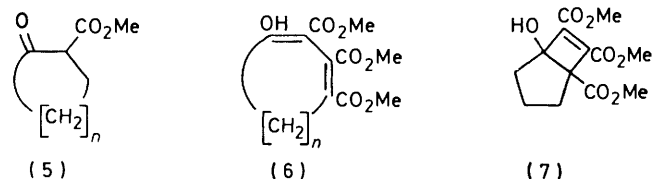
Thirdly, some benzocycloalkanones were examined. The 5-, 6-, and 7-membered-ring β -ketoester (12; $n = 1-3$, R = H) anions furnished crystalline adducts in 60% yield. For reasons similar to those given above, these were formulated as the products of ring-expansion (13; $n = 1-3$, R = H). In the 1-tetralone series the product (13; $n = 2$, R = H) yielded the anhydrides



R = H). Subsequently, reaction of (1; R = Cl) was studied and shown by *X*-ray methods² to yield (3; R = Cl) which existed entirely in the enolic form (4; R = Cl). We report here on the application of this novel ring-expansion procedure to a selection of carbocyclic β -ketoesters.

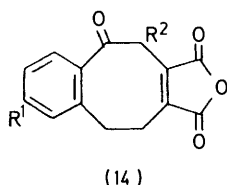
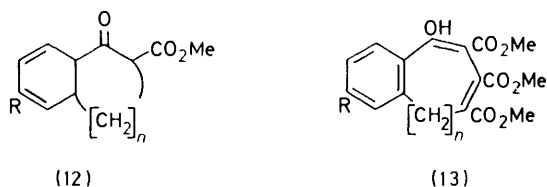
RESULTS AND DISCUSSION

Firstly, commercially available 2-methoxycarbonylcyclopentanone (5; $n = 3$) was converted into the anion using sodium hydride in toluene and was then allowed to react with dimethyl acetylenedicarboxylate (DMAD). The product (50%) was crystalline and formulae (6; $n = 3$), (7), (8), and (9) were considered for it. Lack of vinyl absorption in the ¹H n.m.r. spectrum rules structures (8) and (9) out of consideration, while the ubiquitous enolic absorption at around δ 12 and ability to form a copper complex, eliminates structure (7) and confirms (6; $n = 3$) as the structure of our product as expected from the previous data on compound (4; R = Cl). ¹³C

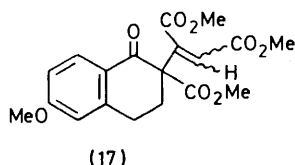


(14; R¹ = H, R² = H or CO₂Me) on hydrolysis depending upon the conditions employed. The structure of (14; R¹ = H, R² = CO₂Me) was confirmed when it was obtained from (14; R¹ = R² = H) by reaction with dimethyl carbonate.

Thus one may say that this two-carbon atom ring-expansion of carbocyclic β -ketoesters exhibits some generality and functions in acceptable yield. The products obtained using DMAD are, however, a little over-functionalised and so we have studied the reactions of two representative β -ketoester sodium salts with methyl propiolate. 2-Methoxycarbonylcyclopentanone (5; $n = 3$) and 2-methoxycarbonyl-1-tetralone (12;



$n = 2$, $R = H$) each gave, in 40% yield, a single adduct when their sodium salts were allowed to react with methyl propiolate. Each contained two methoxycarbonyl groups and had enolic protons (δ ca. 12) as in previous cases; accordingly they were formulated as (15) and (16; $R^1 = Me$, $R^2 = CO_2Me$, $R^3 = H$). Hydrolysis of the latter yielded a keto-acid (16; $R^1 = R^2 = R^3 = H$) which is to be expected from this mode of ring-expansion. The alternative mode would give a diester which on



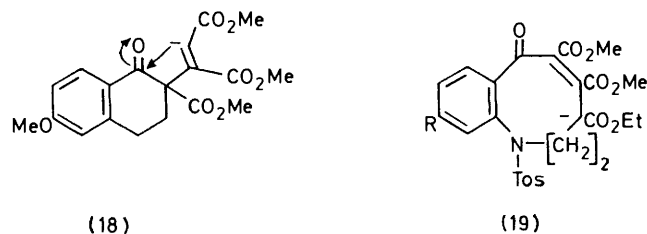
hydrolysis should yield an anhydride (14; $R^1 = R^2 = H$) by analogy with reactions described above.

Significantly, when 6-methoxy-2-methoxycarbonyl-1-tetralone (12; $R = OMe$; $n = 2$) sodium salt was

allowed to react with methyl propiolate, the product (16; $R^1 = Me$, $R^2 = CO_2Me$, $R^3 = OMe$) was obtained in only 20% yield along with the 'Michael' adduct (17) in 20% yield. In spite of the reduced yields, ring-expansion with methyl propiolate is a viable method of introducing functionality at a distant position from the carbonyl group of cyclanones.

It might be expected that phase-transfer catalysts might have a favourable effect on the reaction of β -ketoester salts with acetylene esters: however, addition of the ether 18-crown-6 had no effect whatever on the yield obtained in the ring-expansion of 2-methoxycarbonylcyclopentanone salt with DMAD; on the other hand, dilution of the reaction mixture by 10-fold gave an increase in yield from 50 to 59%.

Mechanistically the present ring-expansion procedure appears similar to the well-known enamine and enol-ether ring-expansions with acetylenic esters.³⁻¹³ An elegant example is to be found in the synthesis of a steganone analogue.¹⁴ The first stage of these reactions involves formally a [2 + 2] cycloaddition [*e.g.* to (2)]; in our work such an intermediate (protonated form) has never been found although Doyle¹⁵ has isolated similar cyclobutene adducts in enol-ether ring expansions. In any event it is inappropriate to invoke orbital symmetry arguments¹⁶ since this is a polar reaction; in particular we note the divergence of product found in ring-expansion of (12; $n = 2$, $R = OMe$) which is suggestive of an intermediate anion (18). Cyclisation as shown (18)



would be inhibited by the methoxy-group, allowing eventual capture of the intermediate by a proton to give the 'Michael' adduct (17). The second stage in all of these ring-expansions *could* be regarded as an orbital-symmetry allowed conrotatory¹⁶ cyclobutene-butadiene cycloreversion. However, this would involve great strain in the transition state where comparatively small (five- and six-membered) rings are fused to cyclobutene. Since we find no change in yield with change of ring size, we reject the concept of a concerted reaction and prefer the simple polar concept leading from (2, arrows) to (19). Charge delocalisation in the latter might provide the driving force for the reaction along with relief of steric crowding. This interpretation is in accord with views presented by Mukaiyama in considering ring-expansion of sulphonium ylides.¹⁷

Finally we point out that this new ring-expansion procedure complements those employing enamines and enol-ethers of cyclic ketones in that it provides (using methyl propiolate) a route to keto-acids in which the

functional groups are separated by three carbon atoms, whereas the former procedures led to separation by two carbon atoms (using DMAD). In cases where β -ketoesters are not directly available (*e.g.* from Dieckmann reactions) it is convenient to proceed from the ketones by conventional base-catalysed reactions with dimethyl carbonate.¹⁸ Since base was required also for the ring-expansion, we investigated the feasibility of a 'one-pot' reaction: in the case of cyclohexanone the yield of (6, $n = 4$) was 35%. This compares favourably with the yield (40%) obtained in two steps when account is taken of savings in time and materials. In all cases, most of the remaining materials are intractable and highly polar.

EXPERIMENTAL

*General Procedure for the Preparation of β -Ketoesters from Cyclic Ketones.*¹⁸—In an atmosphere of nitrogen, sodium hydride (50% dispersion; 2 mol) was placed under anhydrous toluene and to the stirred suspension was added dimethyl carbonate (3 mol) in one portion. The mixture was heated to 80 °C and with continued stirring the ketone (1 mol) was added dropwise during 1 h. When the evolution of hydrogen had ceased, typically after about 3 h, the sodium salt was cooled to 0–5 °C and glacial acetic acid then cautiously run in. Ice–water–2M HCl was added and the aqueous layer separated and washed with toluene (3 \times). The organic phase was then washed with sodium hydrogen-carbonate and water, dried (Na₂SO₄), and evaporated under reduced pressure to give essentially pure product, which may subsequently be distilled or crystallised to separate it from any unreacted ketone.

1-Hydroxy-2,3,4-trimethoxycarbonylcyclohepta-1,3-diene (6; $n = 3$).—To sodium hydride (80% dispersion; 6.0 g, 0.2 mol) in anhydrous toluene (300 cm³) under a nitrogen atmosphere, was added 2-methoxycarbonylcyclopentanone (21.3 g, 0.15 mol) with stirring over 0.5 h. When the addition had been completed, the resultant white paste was stirred at room temperature for 1 h and then cooled to 0–5 °C. With continued stirring, dimethyl acetylenedicarboxylate (23.43 g, 0.165 mol) was added during 1 h keeping the temperature of the reaction mixture below 10 °C. After 4 h at this temperature, the reaction now was shown by t.l.c. to be complete and the reaction liquor was cooled in ice before adding glacial acetic acid (60 cm³) dropwise. Ice–water–2M HCl (100 cm³) was then run in and the aqueous layer separated and washed with toluene (3 \times 100 cm³). The organic phase was washed with water (100 cm³), dried (Na₂SO₄), and evaporated under reduced pressure to yield dark red gum which crystallised as *colourless prisms* of the product (22 g, 51%), m.p. (methanol) 106 °C (Found: C, 54.8; H, 5.8. C₁₃H₁₆O₇ requires C, 54.9; H, 5.7%); δ_{H} 12.9 [1 H, s, OH (exchangeable)], 3.79 (3 H, s, OCH₃), 3.73 (6 H, s, OCH₃), and 2.38 (6 H, br s, –CH₂); ν_{max} (Nujol) 3 500–2 500 (br, OH, chelated), 1 730, 1 715 (C=O), 1 650 (C=O, H-bonded), 1 609, 1 585 cm⁻¹ (C=C), δ_{C} 181.89, 170.61, 168.67, 166.97, 138.27, 134.26, 98.53, 51.75, 51.63, 51.33, 33.07, 31.0, and 27.73.

In a similar fashion, the following were prepared:

(a) 1-Hydroxy-2,3,4-trimethoxycarbonylcyclo-octa-1,3-diene (6; $n = 4$) as *colourless prisms* (30 g, 50%), m.p. (methanol) 91.5–92.5 °C [Found: C, 56.8; H, 6.1%; M^+ , 298.104 4. C₁₄H₁₈O₇ requires C, 56.4; H, 6.1%; M , 298.105 2]; δ_{H} 12.8 [1 H, s, OH (exchangeable)], 3.72 (3 H,

s, OCH₃), 3.65 (6 H, s, OCH₃), 1.10–2.80 (8 H, m, CH₂); ν_{max} (Nujol) 3 500–2 500 (br OH, chelated), 1 730 (C=O), 1 640 cm⁻¹ (C=O, H-bonded).

(b) 1-Hydroxy-2,3,4-trimethoxycarbonylcyclonona-1,3-diene (6; $n = 5$) as *colourless prisms* (16 g, 51%), m.p. (methanol) 112.5–113.5 °C (Found: C, 57.8; H, 6.6. C₁₅H₂₀O₇ requires C, 57.7; H, 6.5%); δ 12.66 [1 H, s, OH (exchangeable)], 3.77 (3 H, s, OCH₃), 3.74 (3 H, s, OCH₃), 3.68 (3 H, s, OCH₃), 3.00–2.05 (4 H, m, –CH₂–), and 2.00–1.00 (6 H, m, –CH₂); ν_{max} (Nujol) 3 500–2 500 (br, OH, chelated), 1 735, 1 720 (C=O), 1 640 (C=O, H-bonded), and 1 610 cm⁻¹ (C=C).

(c) 1-Hydroxy-2,3,4-trimethoxycarbonylcyclodeca-1,3-diene (6; $n = 6$) as *colourless prisms* (8 g, 49%), m.p. (methanol) 103–104 °C (Found: C, 59.0; H, 6.65. C₁₆H₂₂O₇ requires C, 58.9; H, 6.7%); δ 12.79 (1 H, s, OH, exchangeable), 3.74 (3 H, s, OCH₃), 3.66 (3 H, s, OCH₃), 3.64 (3 H, s, OCH₃), 2.80–2.00 (4 H, m, –CH₂–), and 1.86–0.90 (8 H, m, –CH₂–); ν_{max} (Nujol) 3 300–2 500 (OH, chelated), 1 730 (C=O), 1 655 (H-bonded ester), and 1 610 cm⁻¹ (C=C).

(d) 1-Hydroxy-2,3,4-trimethoxycarbonylcyclotetradeca-1,3-diene (6; $n = 10$) as *colourless prisms* (1.9 g, 50%), m.p. (methanol) 76–78 °C (Found: C, 63.0; H, 8.2. C₂₀H₃₀O₇ requires C, 62.8; H, 7.9%); δ 12.90 (1 H, s, OH, exchangeable), 3.74 (3 H, s, OCH₃), 3.71 (3 H, s, OCH₃), 3.65 (3 H, s, OCH₃), 3.50–2.0 (4 H, m, –CH₂–), 2.0–1.0 (16 H, m, –CH₂–); ν_{max} (Nujol) 3 500–2 500 (br, OH, chelated), 1 738, 1 715 (C=O), and 1 660 cm⁻¹ (C=O, H-bonded).

9-Hydroxy-6,7,8-trimethoxycarbonyl-5H-benzocycloheptene (13; R = H, $n = 1$).—In an atmosphere of nitrogen, sodium hydride (50% dispersion; 0.96 g, 0.02 mol) was placed in anhydrous toluene (50 cm³) and to the stirred suspension was added 2-methoxycarbonylindan-1-one (2.85 g, 0.015 mol) in toluene (20 cm³) during 0.5 h. After the addition had been completed, stirring was continued for a further 1 h at room temperature and the sodium salt was cooled to 0–5 °C. Dimethyl acetylenedicarboxylate (2.84 g, 0.02 mol) was now added over 1 h with the temperature being kept below 10 °C, after which time it was permitted to rise to room temperature. After 3 h at room temperature, the reaction mixture was cooled in ice, and glacial acetic acid (5 cm³) was slowly run in. Ice–water–2M HCl (5 cm³) was then added and the aqueous layer was washed once with water (25 cm³), dried (Na₂SO₄), and evaporated under reduced pressure to leave a dark red gum which failed to crystallise, and was shown by t.l.c. to contain one major and several minor components. Initial purification was achieved by chromatography on a short-path pressure column on 50 TLC silica gel [eluant ethyl acetate–light petroleum (60–80 °C) (1:4)] and this afforded a lemon powder. Recrystallisation gave the *product* as *colourless prisms*, (2.7 g, 60%), m.p. (methanol) 118–120 °C (Found: C, 61.4; H, 4.7. C₁₇H₁₆O₇ requires C, 61.4; H, 4.9%); δ 13.8 (1 H, s, OH, exchangeable), 8.10–7.70 (1 H, m, aromatic), 7.70–7.00 (3 H, m, aromatic), 3.85 (3 H, s, OCH₃), 3.77 (3 H, s, OCH₃), 3.75 (3 H, s, OCH₃), and 3.85–3.75 (2 H, m, CH₂); ν_{max} (Nujol) 3 300–2 500 (br, OH, chelated), 1 740, 1 720 (C=O), 1 654 (C=O, H-bonded), and 780 cm⁻¹ (*o*-disubstituted aromatics).

5,6-Dihydro-10-hydroxy-7,8,9-trimethoxycarbonylbenzocyclo-octane (13; R = H, $n = 2$).—To sodium hydride (80% dispersion; 0.512 g, 0.027 mol) in anhydrous toluene (40 cm³) under a nitrogen atmosphere, was added 2-methoxycarbonyl-1-tetralone (4.08 g, 0.02 mol) with stirring during 0.5 h. When addition had been completed, the resultant

yellow paste was cooled to 0–5 °C. Dimethyl acetylenedicarboxylate (3.12 g, 0.022 mol) was added over 0.5 h with the temperature being kept below 10 °C and the reaction mixture was then stirred at room temperature for 6 h. Glacial acetic acid (5 cm³) was run in slowly followed by ice–water–2M·HCl (5 cm³) and the aqueous layer was separated and washed with toluene (3 × 25 cm³). The organic layer was washed once with water (25 cm³), dried (Na₂SO₄), and evaporated under reduced pressure to leave a reddish gum which crystallised on chilling. Recrystallisation gave the *product* (4.1 g, 59%), m.p. (methanol) 101–103 °C (Found: C, 62.6; H, 5.2. C₁₈H₁₆O₇ requires C, 62.5; H, 5.2%); δ 13.2 [1 H, s, OH (exchangeable)], 7.60–7.00 (4 H, m, aromatic), 3.73 (3 H, s, OCH₃), 3.63 (3 H, s, OCH₃), 3.55 (3 H, s, OCH₃), and 3.60–2.40 (4 H, m, CH₂); ν_{max.} (Nujol) 3 300–2 500 (br, OH, chelated), 1 720 (C=O), 1 630 (C=O, H-bonded), and 790 cm⁻¹ (*o*-disubstituted aromatic).

5,6,9,10-Tetrahydro-6-methoxycarbonyl-5-oxobenzocyclo-octene-7,8-dicarboxylic Acid Anhydride (14; R¹ = H, R² = CO₂Me).—To the previous compound (1.73 g, 0.005 mol) was added sodium hydroxide (2N; 20 cm³) and ethanol (25 cm³). The mixture was stirred for 16 h at room temperature, poured into an excess of 2N hydrochloric acid, and extracted with ether. The solvent was then dried (Na₂SO₄), and evaporated under reduced pressure to leave an off-white powder (1.1 g; 73%) which was recrystallised to give the *product* as short *colourless prisms*, m.p. (toluene) 160.5–162 °C (Found: C, 63.8; H, 4.2. C₁₆H₁₂O₆ requires C, 64.0; H, 4.4%); δ 13.65 (1 H, s, OH exchangeable), 7.80–7.15 (4 H, m, aromatic), 3.90 (3 H, s, OCH₃), and 3.0–2.0 (4 H, m, CH₂); ν_{max.} (Nujol) 1 828, 1 760 (anhydride), and 1 665 cm⁻¹ (C=O, H-bonded).

5,6,9,10-Tetrahydro-5-oxobenzocyclo-octene-7,8-dicarboxylic Acid Anhydride (14; R¹ = R² = H).—Compound (13; R = H, *n* = 2) (5.19 g, 0.015 mol), glacial acetic acid (120 cm³), water (18 cm³), and concentrated hydrochloric acid (18 cm³) were refluxed for 72 h, after which evaporation under reduced pressure gave an off-white powder (2.3 g, 67%) which recrystallised to give the *product* as *colourless crystals*, m.p. (toluene) 181.5–183 °C (Found: C, 68.6; H, 4.3. C₁₄H₁₀O₄ requires C, 69.4; H, 4.2%); δ 7.90–6.10 (4 H, m, aromatic), 5.88 (0.4 H, s, OH), 4.15 (1.6 H, s, CH₂), and 3.95–2.08 (4 H, m, CH₂); ν_{max.} (Nujol) 3 600–2 500 (OH), 1 850, 1 770 (anhydride), 1 685, 1 665 (C=O), and 1 595 cm⁻¹ (C=C).

6,7-Dihydro-12-hydroxy-9,10,11-trismethoxycarbonylbenzocyclononene (13; R = H, *n* = 3).—The standard procedure (above) applied to 2-methoxycarbonyl-1-benzosuberone (1.09 g, 0.005 mol) gave the *product* (1.1 g, 61%), m.p. (methanol) 128–129.5 °C (Found: C, 63.7; H, 5.8. C₁₉H₂₀O₇ requires C, 63.3; 5.6%); δ 12.87 [1 H, s, OH (exchangeable)], 7.50–7.00 (4 H, m, aromatic), 3.80 (3 H, s, OMe), 3.62 (3 H, s, OMe), 3.60 (3 H, s, OMe), and 3.00–1.05 (6 H, m, CH₂); ν_{max.} (Nujol) 3 500–2 500 (OH, chelated), 1 725, 1 720 (C=O, ester), 1 660 (C=O, H-bonded), and 762 cm⁻¹ (disubstituted aromatic).

1-Hydroxy-2,4-bismethoxycarbonylcyclohepta-1,3-diene (15).—Sodium hydride (50% dispersion; 6.0 g, 0.125 mol) was placed in anhydrous toluene (300 cm³) and to this stirred suspension under nitrogen was added 2-methoxycarbonylcyclopentanone (14.2 g, 0.1 mol) during 0.5 h. Stirring was continued for 1 h at room temperature, and the resultant sodium salt was then cooled to 0–5 °C and methyl propiolate (9.2 g, 0.11 mol) was added during 0.5 h with the

temperature being kept below 10 °C. The usual work-up gave the *product* (9 g, 40%) as *colourless prisms*, m.p. (methanol) 70 °C (Found: C, 58.8; H, 6.3. C₁₁H₁₄O₇ requires C, 58.4; H, 6.2%); δ 13.59 [1 H, s, OH (exchangeable)], 7.51 (1 H, s, vinylic), 3.78 (3 H, s, OMe), 3.70 (3 H, s, OMe), 2.60–2.45 (2 H, t, CH₂), and 2.20–1.85 (2 H, m, CH₂); ν_{max.} (Nujol) 3 500–2 500 (OH, chelated), 1 700 (C=O), 1 640 (C=O, H-bonded), and 1 590 cm⁻¹ (C=C).

9,10-Dihydro-6,8-bismethoxycarbonyl-6H-benzocyclo-octene-5-one (16; R¹ = Me, R² = CO₂Me, R³ = H).—To sodium hydride (50% dispersion; 12.8 g, 0.27 mol) in anhydrous toluene (1 300 cm³) under nitrogen, was added 2-methoxycarbonyl-1-tetralone (40.8 g, 0.2 mol) dropwise during 0.5 h. Stirring was continued for 1 h at room temperature and the yellow paste then cooled to 0–5 °C. Methyl propiolate (18.5, 0.22 mol) was then added during 0.5 h with the reaction temperature being kept below 10 °C. The usual work-up gave the *product* (23.6 g, 40%) as *colourless prisms*, m.p. (methanol) 120.5 °C (Found: C, 66.9; H, 5.75. C₁₆H₁₆O₅ requires C, 66.65; H, 5.6%); δ 13.25 [1 H, s, OH (exchangeable)], 7.40–7.00 (5 H, m, aromatic + olefinic), 3.74 (3 H, s, OMe), 3.54 (3 H, s, OMe), and 2.85–2.60 (4 H, m, CH₂); ν_{max.} (Nujol) 3 500–2 500 (OH, chelated), 1 700 (C=O), 1 650 (C=O, H-bonded), and 1 608 cm⁻¹ (C=C).

9,10-Dihydro-8-hydroxycarbonyl-6H-benzocyclo-octene-5-one (16; R¹ = R² = R³ = H).—To the previous compound (5.7 g, 0.02 mol) was added a mixture of glacial acetic acid (120 cm³), concentrated hydrochloric acid (18 cm³), and water (18 cm³). The temperature was raised to 70 °C and the reaction mixture then stirred for 2 h. T.l.c. indicated a substantial quantity of starting material remaining and the temperature was increased to 90 °C and kept at this temperature for 6 h. The reaction mixture was cooled to room temperature and extracted with ether (3 × 100 cm³), washed with water (100 cm³), dried (Na₂SO₄), and evaporated to dryness under reduced pressure. Recrystallisation of the yellow powder gave the *product* (3 g, 70%) as *needles*, m.p. (ethanol) 209–210 °C (Found: C, 72.5; H, 5.2%; M⁺, 216.077 6. C₁₃H₁₂O₃ requires C, 72.2; H, 5.55%; M, 216.078 6); δ 7.60–7.00 (5 H, m, aromatic plus exchangeable OH), 6.79–6.58 (1 H, t, olefinic), 3.78–3.69 (2 H, d, CH₂), 3.29–2.05 (2 H, t, CH₂), and 2.90–2.65 (2 H, t, CH₂); ν_{max.} (Nujol) 3 400–2 400 (OH, broad), 1 730 (C=O, carbonyl), and 1 700 cm⁻¹ (C=O).

Reaction of Methyl 1,2,3,4-Tetrahydro-6-methoxy-1-oxonaphthalene-2-carboxylic Acid (12; R = OMe, *n* = 2) with Methyl Propiolate.—To sodium hydride (50% dispersion; 1.28 g, 0.027 mol) in anhydrous toluene (50 cm³) under nitrogen, was added the title compound (4.68 g, 0.02 mol) with stirring over 1 h. When the addition had been completed, the sodium salt was stirred for a further 1 h at room temperature and then cooled to 0–5 °C. Methyl propiolate (1.85 g, 0.022 mol) was added during 1 h with the temperature being kept below 10 °C; after this time, t.l.c. indicated that a considerable quantity of starting material remained. The reaction mixture was stirred for 16 h at room temperature and then glacial acetic acid (5 cm³) was run in slowly followed by ice–water–2M HCl (5 cm³) whereupon the aqueous layer was separated and washed with toluene (3 × 25 cm³). The bulked organic layer was washed once with water (25 cm³), dried (Na₂SO₄), and evaporated under reduced pressure to leave a reddish gum which failed to crystallise. T.l.c. indicated that this gum contained, along with a large quantity of polar material, two major components and these were separated using short-

path pressure column chromatography with a silica support. The eluant was ethyl acetate-light petroleum (60–80 °C) (1:4) and this led to the isolation of, firstly 9,10-dihydro-2-methoxy-6,8-bismethoxycarbonyl-6H-benzocyclo-octen-5-one (16; R¹ = Me, R² = CO₂Me, R³ = OMe) (1.3 g, 21%) as colourless needles, m.p. (methanol) 126.5–128 °C (Found: C, 64.15; H, 5.7. C₁₇H₁₈O₆ requires C, 64.1; H, 5.7%); δ 13.46 [1 H, s, OH (exchangeable)], 7.31–6.57 (4 H, m, aromatic plus vinylic proton), 3.80 (3 H, s, OMe), 3.74 (3 H, s, OMe), 3.61 (3 H, s, OMe), and 3.20–2.60 (4 H, m, CH₂); ν_{max.} (Nujol) 1 730 (C=O, ester), 1 665 (C=O, H-bonded), and 1 610 cm⁻¹ (C=C). This was followed from the column by methyl 1,2,3,4-tetrahydro-6-methoxy-2-methoxycarbonyl-2-[1,2-bis(methoxycarbonyl)vinyl]-1-oxonaphthalene-2-carboxylate (17) (1.25 g, 20%) as short colourless prisms, m.p. 123–124.5 °C (methanol) (Found: C, 64.5; H, 5.5. C₁₇H₁₈O₆ requires C, 64.1; H, 5.7%); δ 7.91 (1 H, s, vinylic proton), 7.60–7.44 [2 H, m, aromatic (7-H, 8-H)], 6.74–6.60 (2 H, m, aromatic plus vinylic proton), 3.85 (3 H, s, OMe), 3.82 (3 H, s, OMe), 3.75 (3 H, s, OMe), and 2.80 (4 H, m, CH₂); ν_{max.} (Nujol) 1 725 (C=O, ester) and 1 600 cm⁻¹ (C=C).

The 'One-pot' Conversion of Cyclohexanone into 1-Hydroxy-2,3,4-trismethoxycarbonylcyclo-octa-1,3-diene.—Sodium hydride (50% dispersion; 19.2 g, 0.4 mol) was placed in anhydrous toluene (1 000 cm³) under nitrogen and to this was added dimethyl carbonate (54 g, 0.6 mol). The mixture was heated to 80 °C and cyclohexanone (19.6 g, 0.2 mol) was run in over 1 h with stirring. Stirring was continued at this temperature for 3 h and excess of dimethyl carbonate distilled out before cooling to 0–5 °C and adding dimethyl acetylenedicarboxylate (31.2 g, 0.22 mol) during 0.5 h. After 4 h at <10 °C glacial acetic acid (40 cm³) was added followed by ice-water-2N HCl (60 cm³) and the aqueous layer then separated and washed with toluene (3 × 50 cm³). The combined organic phase was washed once with water (50 cm³), dried (Na₂SO₄), and evaporated under reduced pressure to leave a red gum which crystallised to give the product as colourless prisms (21 g, 35%), identified by mixed m.p. and i.r. spectroscopy.

Reaction of 2-Methoxycarbonylcyclopentanone with Dimethyl Acetylenedicarboxylate including 18-Crown-6.—Compound (6; n = 3) was prepared as previously described (10% scale) with the exception that when the initial sodium salt had formed, 18-crown-6 (50 mg) was added. A control experiment was set up on the same scale without the 18-crown-6. Both reactions produced 1-hydroxy-2,3,4-trismethoxycarbonylcyclohepta-1,3-diene (2 g), identified by mixed m.p. and i.r.

1-Oxo-cyclo-oct-3-ene-3,4-dicarboxylic Acid Anhydride (10).—To 1-hydroxy-2,3,4-trismethoxycarbonylcyclo-octa-1,3-diene (6; n = 4) (2.0 g, 0.66 mol) was added glacial acetic acid (6 cm³) and concentrated hydrochloric acid (6 cm³). The reagents were heated at reflux for 48 h, then cooled and diluted with a large volume of water, extracted with chloroform (2 × 25 cm³), dried (Na₂SO₄), and evaporated to dryness leaving an off-white powder as the product (0.5 g, 40%). This yield was improved (60%) when instead of extracting with chloroform, the reaction mixture was, on cooling, evaporated to dryness directly to afford the anhydride, m.p. (toluene) 136 °C (Found: C, 61.8; H, 5.4%; M⁺, 194.0578. C₁₀H₁₀O₄ requires C, 61.9; H, 5.2%; M, 194.0579); δ 3.54 (2 H, s, CH₂), 2.65–2.45 (4 H, m, CH₂), and 2.05–1.75 (4 H, m, CH₂); ν_{max.} (Nujol) 1 850, 1 830, 1 780 (anhydride), and 1 700 cm⁻¹ (C=O).

Dimethyl 6,7,8,9-Tetrahydro-3-hydroxy-2H-cyclo-octa[c]-

pyrazole-4,5-dicarboxylate (11; n = 4, H instead of Ph).—Hydrazine hydrate (0.2 g, 0.004 mol), glacial acetic acid (1 cm³), and 1-hydroxy-2,3,4-trismethoxycarbonylcyclo-octa-1,3-diene (1 g, 0.003 mol) were mixed and heated at 90 °C for 2 h. The resultant red syrup was cooled and ultimately deposited crystals of the product (0.9 g, 90%), recrystallised as reflective plates, m.p. (methanol) 216–217 °C (Found: C, 55.9; H, 5.8; N, 10.0%; M, 280.1057. C₁₃H₁₆N₂O₅ requires C, 55.8; H, 5.8; N, 10.0%; M, 280.1059); δ [(CD₃)₂SO] 12–10.00 (2 H, br, NH and OH), 3.61 (3 H, s, OMe), 3.58 (3 H, s, OMe), 2.60–2.20 (4 H, m, CH₂), and 2.00–1.40 (4 H, m, CH₂); ν_{max.} (Nujol) 3 290 (NH), 2 700–2 300 (OH), 1 705 (C=O), and 1 605 cm⁻¹ (C=C).

Dimethyl 6,7,8,9-Tetrahydro-3-hydroxy-2-phenyl-2H-cyclo-octa[c]pyrazole-4,5-dicarboxylate (11; n = 4).—To phenylhydrazine (1.2 g, 0.012 mol) and glacial acetic acid (10 cm³) was added 1-hydroxy-2,3,4-trimethoxycarbonylcyclo-octa-1,3-diene (2.98 g, 0.01 mol). This mixture was heated for 4 h at 95 °C and a red syrup formed, which was poured into ice-water. The resultant precipitate was collected on a filter (3.1 g, 84%), and recrystallised as colourless crystals, m.p. (methanol) 180–181.5 °C (Found: C, 64.3; H, 5.8; N, 7.95%; M⁺, 356.1357. C₁₈H₂₀N₂O₅ requires C, 64.1; H, 5.7; N, 7.9%; M, 356.1372); δ 12.00–11.00 (1 H, br, s, OH), 7.90–7.10 (5 H, m, aromatic), 3.80 (6 H, 2 × s, OMe), 3.00–2.20 (4 H, m, CH₂), and 2.00–1.50 (4 H, m, CH₂); ν_{max.} (Nujol) 3 200–2 200 (OH, chelated), 1 734, and 1 720 cm⁻¹ (C=O, ester). The following were similarly prepared:

(a) *Dimethyl 7,8-dihydro-3-hydroxy-2H,6H-cyclohepta-[c]pyrazole-4,5-dicarboxylate* (11; n = 3): colourless prisms, m.p. (methanol) 167–168 °C (Found: C, 62.8; H, 5.4; N, 8.05. C₁₈H₁₈N₂O₅ requires C, 63.2; H, 5.3; N, 8.2%); δ 12.00–11.60 (1 H, br s, OH), 7.90–7.10 (5 H, m, aromatic), 3.88 (3 H, s, OMe), 3.78 (3 H, s, OMe), 3.00–2.50 (4 H, m, CH₂), and 2.40–1.80 (2 H, m, CH₂); ν_{max.} (Nujol) 3 110 (OH), 1 710, 1 690 (C=O), and 1 655 cm⁻¹ (H-bonded C=O).

(b) *Dimethyl 7,8,9,10-tetrahydro-3-hydroxy-2-phenyl-2H,6H-cyclonona[c]pyrazole-4,5-dicarboxylate* (11; n = 5): colourless crystals, m.p. (methanol) 203–205 °C (Found: C, 64.6; H, 6.1; N, 7.5. C₂₀H₂₂N₂O₅ requires C, 64.8; H, 6.0; N, 7.6%); δ 10.00–7.00 (6 H, m, aromatic plus OH), 3.80 (3 H, s, OMe), 3.68 (3 H, s, OMe), 2.90–2.10 (4 H, m, CH₂), and 2.00–1.20 (6 H, m, CH₂); ν_{max.} (Nujol) 3 400–3 100 (OH), 1 712 (C=O), and 1 690 cm⁻¹ (C=O).

(c) *Dimethyl 6,7,8,9,10,11-hexahydro-3-hydroxy-2-phenyl-2H-cyclodeca[c]pyrazole-4,5-dicarboxylate* (11; n = 6): colourless prisms (550 mg, 42%), m.p. (methanol) 274–249 °C (Found: C, 65.5; H, 6.2; N, 7.2. C₂₁H₂₄N₂O₅ requires C, 65.6; H, 5.8; N, 7.3%); δ 11.50–10.00 (1 H, br s, OH), 7.90–7.60 (2 H, m, aromatic), 7.60–7.30 (3 H, m, aromatic), 3.80 (3 H, s, OMe), 3.79 (3 H, s, OMe), 2.90–2.20 (4 H, m, CH₂), and 2.00–0.70 (8 H, m, CH₂); ν_{max.} (Nujol) 3 400–3 100 (OH), 1 730, 1 715 (C=O, ester), and 1 660 cm⁻¹ (H-bonded C=O).

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