

Bridged Ring Systems. Part 19.¹ Condensation–Cyclisation Reaction of Acrylaldehyde with Diethyl 2,5-Dioxocyclohexane-1,4-dicarboxylate

By Geo. L. Buchanan,* William B. Kennedy, and Alex. M. Lawson, Department of Chemistry, University of Glasgow, Glasgow G12 8QQ

The title reaction gave a tricyclic dioxo-diester (6) and a pair of epimeric tetracyclic alcohols (12).

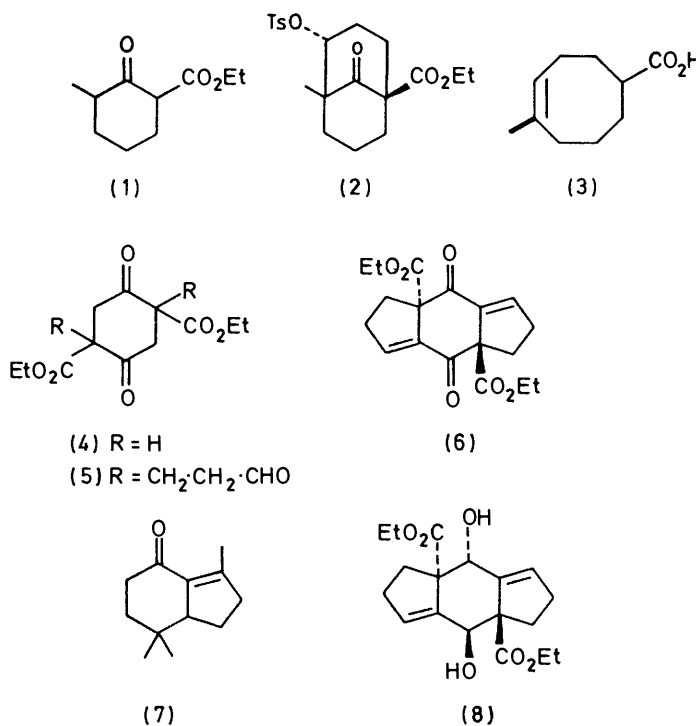
EARLIER papers^{1,2} in this series have described the use of bridged bicyclic intermediates in ring-expansion reactions [e.g. (1) → (3) via (2)]. We now report an attempt to bring about a double ring-expansion of the bis-β-oxo-ester (4).

Diethyl 2,5-dioxocyclohexane-1,4-dicarboxylate (4) was treated with acrylaldehyde under conditions which were expected³ to promote cyclisation of the intermediate Michael adduct (5). Two new crystalline products were obtained. The first (A), C₁₈H₂₀O₆, was readily identified as the dioxo-diester (6) on spectroscopic grounds (see Experimental section), notably by its simple ¹H n.m.r. and its mass spectrum, whose base peak at *m/e* 166 indicated symmetrical fission. The u.v. absorption

265 nm (ϵ 8 173)]. On reduction (NaBH₄) the product (A) afforded the diol (8) which showed the expected spectral features (see Experimental section). The formation of two *cis*-β-hydroxy-ester systems is indicated by the i.r. spectrum, which shows intramolecular H-bonding, but the relative geometry of the two ester groups in (6) and in (8) cannot be assigned with confidence. The diacid derived from (8) could not be induced to form a γ-lactone, and on this basis the *trans*-configuration is preferred.

The second crystalline product (B) was isomeric with (5). It showed hydroxy, ester, and ketone i.r. bands but no u.v. absorption. No free aldehyde function could be detected (¹H n.m.r.) in neutral or acidic media. Closer inspection of the ¹H n.m.r. spectrum showed that (B) was a *ca.* 1 : 1 mixture of epimeric alcohols. On adding D₂O, two doublets (each ½ H) at τ 6.15 (*J* 8 Hz) and 6.65 (*J* 10 Hz) disappeared, and two quartets (each ½ H) centred at τ 4.7 and 4.9 collapsed to doublets (*J* 4 and 9 Hz, respectively). Conversely, irradiation at τ 4.7 caused the 6.65 doublet to collapse to a singlet, and irradiation at τ 4.9 similarly simplified the doublet at τ 6.15. The high-field component of these AMX systems (*ca.* τ 7.2) was largely obscured. These findings suggest a hemiacetal system (9), and this was confirmed by oxidation of (B) to a lactone (ν_{CO} 1 771 cm⁻¹). The ¹H n.m.r. spectrum of (B) also showed a 1H multiplet at τ 4.35 which was initially mistaken † for a vinylic H signal. In the spectrum of the derived lactone the same signal was displaced to τ 4.08, but its ¹³C n.m.r. spectrum (see Table) showed only one signal [101 p.p.m. (d in off-resonance decoupled spectrum)] in the vinylic C region and so all structures which include a C=C system can be neglected. The n.m.r. data are most plausibly assigned to an acetal system (10); accordingly the lactone is formulated as (11) and (B) as a mixture of lactols (12).

Structure (11) is fully consistent with the ¹³C n.m.r. spectrum and the high ν_{CO} value is consonant with a δ-lactone system locked in the boat configuration.⁵ Indeed the boat configuration of the dioxabicyclo[3.3.1]nonane moiety is also indicated by our earlier observation that the lactol (12) existed as a 1 : 1 mixture of epimers. Were it in the alternative chair–chair configuration, the *endo*-OH orientation would be sterically disfavoured⁶ and a 1 : 1 ratio would be unlikely under conditions of



[λ_{max} , 235 (ϵ 4 960) and 264 nm (ϵ 8 170)] is abnormal: the lower wavelength maximum is in approximate agreement with the calculated value if we assume poor overlap in the enone π -systems. The other maximum is unexpected but is recorded⁴ for the analogue (7) [λ_{max} .

† Reduction of (B) (Pd–C) removed this signal and produced an oily product (C₁₈H₂₆O₇) which has not been identified.

¹ Part 18, G. L. Buchanan and G. A. R. Young, *J.C.S. Perkin I*, 1973, 2404.

² For a review see G. L. Buchanan, *Topics Carbocyclic Chem.*, 1969, 227.

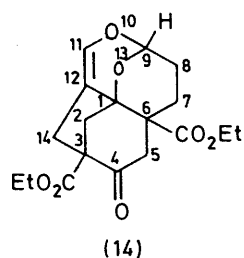
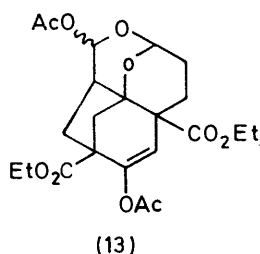
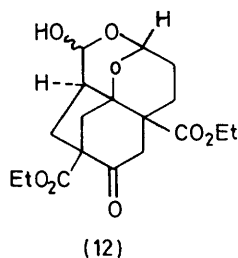
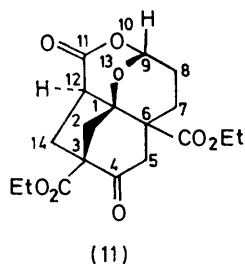
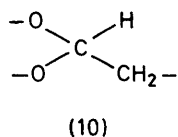
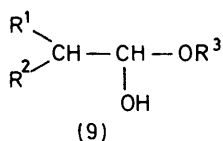
³ G. L. Buchanan and G. W. McLay, *Tetrahedron*, 1966, **22**, 1521.

⁴ J. Wiemann and F. Weisbach, *Compt. rend.*, 1963, **257**, 1486.

⁵ K. K. Cheung, K. H. Overton, and G. A. Sim, *Chem. Comm.*, 1965, 634.

⁶ Ref. 2, p. 217.

thermodynamic control. These data determine the stereochemistry of (11) and (12).



Two further reactions of (B) confirmed its structure. Acetylation yielded a mixture of diacetates (13) in which one of the new functions is an enol acetate [ν_{CO} 1 770 and 1 744 cm^{-1} ; τ 4.7 (s); mass spectral peaks at $M - 44$ and $M - 60$]. Accompanying the diacetates was a dehydration product, more conveniently prepared from (B) by treatment with acid, whose spectral features [τ 3.14 (s); $\nu_{\text{C}=\text{C}}$ 1 690 cm^{-1} ; see Table for ^{13}C n.m.r.] are in agreement with structure (14).

^{13}C N.m.r. data (p.p.m. from Me_4Si) for the lactone (11) and its dehydration product (14) (excluding ester peaks)

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-11	C-12	C-14
(11)	80.7 (s)	32.7 (t)	63.1 (s)	201 (s)	40 (q)	46.7 (s)	27.2 (t)	47.4 (q)	101 (d)	172 (s)	44.3 (d)	25.5 (t)
(14)	76.4 (s)	32.7 (t)	62.0 (s)	203 (s)	40.4 (q)	49.0 (s)	28.7 (t)	46.5 (q)	95 (d)	140 (d)	111 (s)	28.1 (t)

EXPERIMENTAL

Isolation of the Products (A) and (B).—Acrylaldehyde (4.15 g) was added slowly with stirring to an ice-cold solution of diethyl 2,5-dioxocyclohexane-1,4-dicarboxylate (9.5 g) and triethylamine (1 ml) in tetrahydrofuran (400 ml) and stirring was continued for 20 h at room temperature. The solution was then neutralised (AcOH), the excess of tetrahydrofuran was removed *in vacuo*, and the residue, in ether, was washed and dried. Evaporation afforded a pale yellow oil which deposited 2,5-dihydroxyterephthalic acid, and the residue crystallised from ether yielding (A) *diethyl 2,8-dioxotricyclo[7.3.0.0^{3,7}]dodeca-3,9-diene-1,7-dicarboxylate* (6), m.p. 184° (Found: C, 64.85; H, 5.95. $\text{C}_{18}\text{H}_{20}\text{O}_6$ requires C, 65.05; H, 6.05%), m/e 332 and 166 (base peak); τ 3.4 (2 H, t), 5.91 (4 H, q), 8.87 (6 H, t), and 7.0–8.0 (8 H, m); ν_{max} (CCl_4) 1 751, 1 720sh, 1 705, and 1 623 cm^{-1} ; λ_{max} (EtOH) 264 (ϵ 8 170) and 235 nm (4 960); and (B) the *diethyl 11-hy-*

droxy-4-oxo-10,13-dioxatetracyclo[7.3.1.0^{1,6}.1^{3,12}]tetradecane-3,6-dicarboxylates (12), m.p. 132–140° (from ethyl acetate) (Found: C, 58.35; H, 6.15. $\text{C}_{18}\text{H}_{24}\text{O}_8$ requires C, 58.7; H, 6.55%); m/e 368; ν_{max} (CCl_4) 3 632, 3 585w, 1 741, and 1 724 cm^{-1} ; τ 4.4 (1 H, fine m), 4.7 ($\frac{1}{2}$ H, q, J 4 and 10 Hz), 4.9 ($\frac{1}{2}$ H, q, J 8 and 9 Hz), 5.78 (4 H, q), 6.15 ($\frac{1}{2}$ H, d, J 8 Hz), 6.65 ($\frac{1}{2}$ H, d, J 10 Hz), and 8.75 (6 H, t).

The yields of (A) and (B) varied unpredictably from one experiment to another. The residual oil was a complex mixture.

The Lactone (11).—The mixture of alcohols (12) (0.49 g) in acetone (20 ml) was titrated with Jones reagent at 0 °C and taken up in ether; the solution was washed, dried, and evaporated to give the *lactone* (0.37 g), m.p. 158–159° (from ethanol) (Found: C, 59.05; H, 6.15. $\text{C}_{18}\text{H}_{22}\text{O}_8$ requires C, 59.0; H, 6.05%); m/e 366; ν_{max} (CCl_4) 1 770, 1 744, 1 740, 1 724, and 1 614 cm^{-1} ; τ 4.15 (1 H, d, J 5 Hz), 5.74 (2 H, q), 5.78 (2 H, q), 8.68 (3 H, t), and 8.70 (3 H, t).

Reductions.—(a) The alcohol mixture (12) (500 mg) in ethanol (100 ml) was reduced in the presence of 10% Pd-C (500 mg). The oily product, isolated by preparative t.l.c., showed no u.v. absorption; ν_{max} (CCl_4) 3 635, 3 545, 3 460, 1 745, 1 723, and 1 700 cm^{-1} ; τ 5.7 (2 H, q), 5.8 (2 H, q), 6.37 (2 H, t, J 7 Hz), 8.32br (1 H, disappears with D_2O), 8.68 (3 H, t), and 8.72 (3 H, t); m/e 354.1672 (calc. for $\text{C}_{18}\text{H}_{26}\text{O}_7$: 354.1671).

(b) The bis-enone (6) (113 mg) suspended in methanol (40 ml) was stirred with sodium borohydride (50 mg) in water until it passed into solution. Next day the *diol* (8) was precipitated with water; m.p. 150° from ethyl acetate; m/e 336; ν_{max} (CCl_4) 3 480 and 1 706 cm^{-1} , unchanged on dilution; τ 4.05 (2 H, m), 5.84 (4 H, q superimposed on CHOH signals), 7.57 (8 H, m), and 8.79 (6 H, t) (on adding D_2O the signal at 5.84 is partially sharpened); transparent in the u.v. (Found: C, 64.2; H, 7.25. $\text{C}_{18}\text{H}_{24}\text{O}_6$ requires C, 64.25; H, 7.2%).

Hydrolysis by concentrated hydrochloric acid in methanol (20 h; room temperature) afforded the corresponding *diacid*, which sublimed at 120° and 0.01 mmHg; m.p. 163–165° (Found: C, 59.9; H, 5.8. $\text{C}_{14}\text{H}_{16}\text{O}_6$ requires C, 60.0; H, 5.75%); m/e 280; ν_{max} (CHCl_3) 3 600–2 400br, 3 490, and 1 700 cm^{-1} .

Dehydration.—The alcohol (12) (50 mg) and toluene-*p*-sulphonic acid (5 mg) were refluxed overnight in benzene (20 ml) in a Dean-Stark apparatus. The solution was neutralised (K_2CO_3) then washed and evaporated to yield the *vinyl ether* (14) (41 mg), m.p. 131–132° (from ethanol) (Found: C, 62.1; H, 6.0. $\text{C}_{18}\text{H}_{22}\text{O}_7$ requires C, 61.7; H, 6.35%); m/e 350; ν_{max} (CCl_4) 1 750, 1 742, 1 723, and 1 690 cm^{-1} ; τ 3.3 (1 H, fine t), 4.42br (1 H), 5.75 (4 H, q), and 8.65 (6 H, t). The same product was obtained from the alcohol (30 mg) after 3 or 4 days in ethanol (30 ml) containing 5*N*-sulphuric acid (10 ml) followed by refluxing for 1 h.

The Acetates (13).—(a) The alcohol (12) (143 mg) in acetic anhydride (1.5 ml) and dry pyridine (3 ml) was refluxed for 90 min; the mixture was cooled and poured onto ice, yielding the *diacetate* mixture, m.p. 123–125°; m/e 452 (Found: C, 58.65; H, 6.7. $\text{C}_{22}\text{H}_{28}\text{O}_{10}$ requires C, 58.4; H, 6.25%); ν_{max} (CCl_4) 1 770, 1 744, and 1 725 cm^{-1} ; τ 4.05

(1 H, superimposed doublets), 4.4 (1 H, broadened d), 4.7 (1 H, s), 5.75 and 5.83 (4 H, superimposed quartets), 7.85 (3 H, s), 7.93 (3 H, s), and 8.68 and 8.71 (6 H, superimposed triplets).

(b) The alcohol (12) (74 mg) and isopropenyl acetate (8 ml) were refluxed overnight with toluene-*p*-sulphonic acid (5 mg). The mixture was neutralised (K_2CO_3) and concentrated *in vacuo* and the residue extracted into ether. Evaporation yielded a gummy solid which was separated

(preparative t.l.c.) into the vinyl ether (14) and the diacetate mixture.

We are indebted to Mrs. W. Harkness and her staff for microanalyses, Mr. J. Gall for 1H n.m.r. spectra, Mr. A. Ritchie for mass spectra, and Mrs. F. Lawrie for i.r. spectra. We also thank Dr. I. Sadler, Edinburgh University, for the ^{13}C n.m.r. spectra, and the S.R.C. for a grant (to W. B. K.).

[6/1358 Received, 12th July, 1976]
