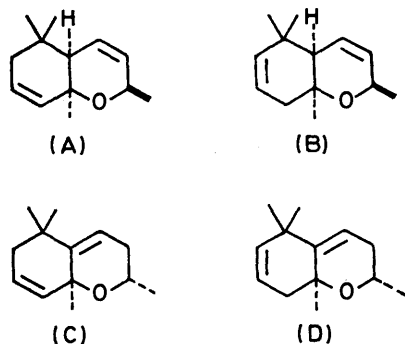


Synthesis and Structure of Edulans I and II

By David R. Adams, Surendra P. Bhatnagar, and Richard C. Cookson,* Chemistry Department, Southampton University, Southampton SO9 5NH

Edulans I and II have been shown by synthesis to be the epimeric 3,5,6,8a-tetrahydro-2,5,5,8a-tetramethyl-2*H*-1-benzopyrans (11) and (10). Diels–Alder addition of penta-1,3-diene to bromomesityl oxide, elimination of hydrogen bromide, and aldol condensation with acetaldehyde produced the hydroxy-ketone (1) already used in the synthesis of β -damascenone, reduction of which gave 1-(2,6,6-trimethylcyclohexa-1,3-dienyl)butane-1,3-diol (3). Cyclisation of this diol (3) with acid led to (\pm)-edulans II, isomerised to (\pm)-edulans I by further treatment with acid. N.m.r. spectrometry at 100 MHz, including use of double irradiation, INDOR, and lanthanide shifts, confirmed the structures of the edulans.

EDULANS I and II, with intense rose-like aromas, are important trace components contributing to the flavour of the purple passionfruit (*Passiflora edulis*, Sims).^{1,2} They were recently shown to be isomeric 2,5,5,8a-tetramethyltetrahydro-1-benzopyrans^{1,2} and from the products of hydrogenation of the small quantities available the C.S.I.R.O. group² suggested that edulan I had structure (A) or (B) with a 3,4-double bond and



edulans II structure (C) or (D) with a 4,4a-double bond. The identity of the mass spectra of the two isomers^{1,2} persuaded us that they were more likely to be stereo-

¹ K. E. Murray, J. Shipton, and F. B. Whitfield, *Austral. J. Chem.*, 1972, **25**, 1921.

isomers than double-bond isomers, so we decided to synthesise the two epimers of structure (C) for comparison with the natural products.

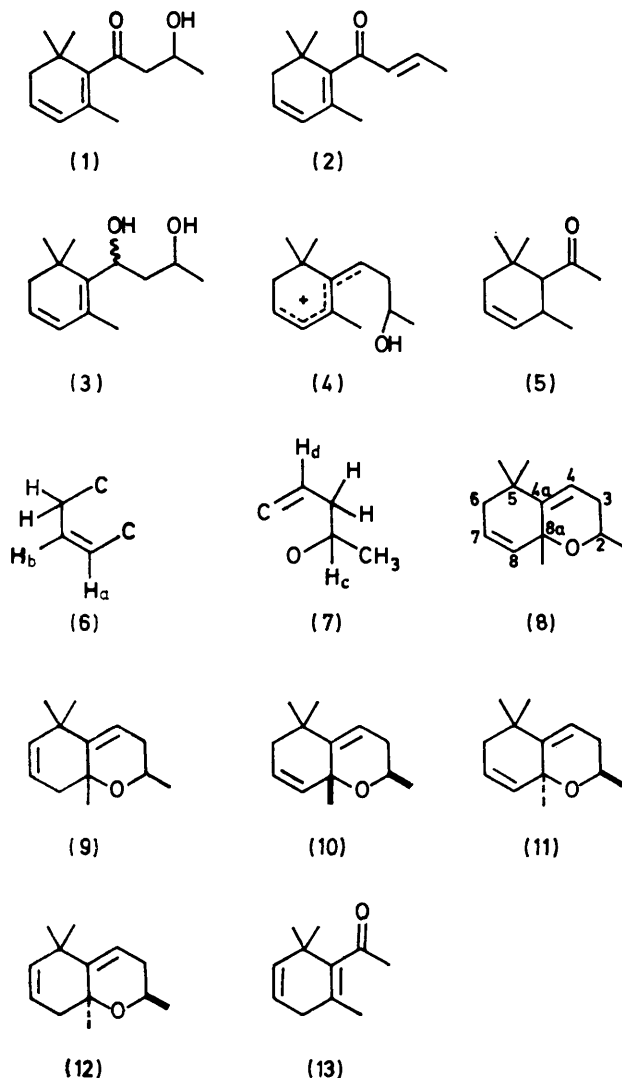
The hydroxy-ketone (1), an intermediate in the synthesis³ of β -damascenone (2), can be made in three steps from bromomesityl oxide in an overall yield of up to 70% (acid-catalysed Diels–Alder reaction with penta-1,3-diene, elimination of hydrogen bromide, and aldol condensation with acetaldehyde). Reduction of the hydroxy-ketone (1) with sodium borohydride in methanol gave the required diol (3) in quantitative yield as a mixture of about equal amounts of the two stereoisomers (estimated from n.m.r.). These diols (3) were treated with 0.5*M*-boron trifluoride in ether for 30 min at 0 °C. G.l.c. analysis on a 5% Carbowax column at 130 °C showed the presence of two major components, X and Y, in the ratio 7 : 2. Longer reaction time or more vigorous conditions resulted in the formation of a greater proportion of Y. Thus treatment of the diols (3) with 0.5*M*-boron trifluoride in ether for 1 h or with the ion-exchange resin IR 120 (H⁺ form) in ether for 3 h gave an equilibrium mixture of X and Y in the ratio 1 : 10, as did treatment of either X or Y under the same conditions.

The agreement of the mass and i.r. spectra of X and Y

² F. B. Whitfield, G. Stanley, and K. E. Murray, *Tetrahedron Letters*, 1973, 95.

³ K. S. Ayyar, R. C. Cookson, and D. A. Kagi, *J.C.S. Chem. Comm.*, 1973, 161.

with those published^{1,2} for edulans II and I indicated that they had the same structures. Careful comparison of the natural and synthetic materials at the C.S.I.R.O. (retention times on several columns, n.m.r. spectra, and



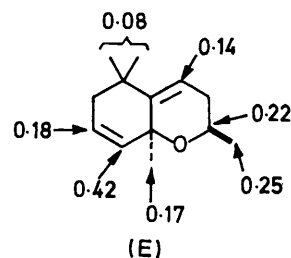
products of microhydrogenation) confirmed that X was edulan II and Y edulan I.⁴ Cyclisation of the diols (3) to the (\pm)-edulans and equilibration of (\pm)-edulan I and (\pm)-edulan II evidently occurs through the intermediate pentadienyl cation (4). Migration of double bonds under such mild conditions would not be expected [compound (5) is stable under much harsher conditions], so that the positions of the double bonds in the products are fixed by those in the cation (4). Thus both edulans must have 4,4a- and 7,8-double bonds and structures (A), (B), and (D) can be eliminated: the edulans must therefore be the

* Details will be published separately by Dr. F. B. Whitfield and Mr. G. Stanley.

† The absolute configuration of the natural edulans is not known; the synthetic compounds are, of course, racemic.

epimeric 3,5,6,8a-tetrahydro-2,5,5,8a-tetramethyl-2H-1-benzopyrans.

Although the positions of the double bonds are clearly indicated by the chemical evidence, spectroscopic confirmation was sought. The position of the disubstituted double bond could not be assigned with certainty from the routine n.m.r. spectra. Comprehensive double-irradiation and INDOR experiments proved the presence of groups (6) and (7) but did not in themselves prove which way round they are joined [(8) or (9)]. However, in the overlapping signals from the two methylene groups, those from group (7) occur at lower field than those from group (6). This is expected from structure (8) but not necessarily from (9). Conclusive evidence for the structures of X and Y (edulans II and I) came from addition of the lanthanide shift reagent $\text{Eu}(\text{fod})_3$ to the n.m.r. solvent; the gradients taken from plots of induced shift *versus* molar ratio of X or Y to added reagent are shown in Table 3. The fact that the protons H_a in (6) undergo the largest shifts proves they must be adjacent to the O atom as in (8), not more than 5 Å away from it as in (9). Examples of the shifts to lower field (in p.p.m.) produced in the various signals on addition of $\text{Eu}(\text{fod})_3$ are given in formula (E).



The configurations of the edulans have been established by hydrogenation to the octahydrobenzopyrans of known configuration;^{2,4} edulan II forms products with the 2- and 8a-methyl groups *cis* and edulan I those with *trans*-methyl groups.* The predominance of edulan I (11) † at equilibrium agrees with the expected greater stability of (11), with the 2-methyl group equatorial in a distorted chair conformation of the dihydropyran ring, than of (12), with the 2-methyl group equatorial in a distorted boat conformation (or axial in a distorted chair).

The product from cyclisation of the diol (1) with acid contained about 2% of a third isomer, Z, with spectroscopic properties consistent with the structure (12). It is believed to have been formed from the small amount of double-bond isomers, including (13), present as impurities in the 1-acetyl-2,6,6-trimethylcyclohexa-1,3-diene used in the synthesis.³

EXPERIMENTAL

N.m.r. spectra (60 MHz) were recorded on a Perkin-Elmer R-12 instrument using carbon tetrachloride as

⁴ D. R. Adams, S. P. Bhatnagar, R. C. Cookson, G. Stanley, and F. B. Whitfield, *J.C.S. Chem. Comm.*, 1974, 469.

solvent and tetramethylsilane as internal reference. N.m.r. spectrometry at 100 MHz, including INDOR and shift reagent experiments, was carried out on a Varian HA-100 spectrometer with deuteriochloroform as solvent. I.r. spectra were obtained on a Perkin-Elmer 157G spectrometer. Mass spectra were recorded at 70 eV on an A.E.I. MS12 spectrometer.

Analytical g.l.c. was performed on a Pye Series 104 Chromatograph (2 m × 4 mm glass column packed with 5% Carbowax 20 M on 80–100 mesh Diatomite C). Preparative g.l.c. was carried out on a 3 m × 6 mm glass column packed with 15% Carbowax 20 M on 60–72 mesh Diatomite C.

Petroleum refers to the fraction of b.p. 40–60°; silica gel was 100–200 mesh.

1-(2,6,6-Trimethylcyclohexa-1,3-dienyl)butane-1,3-diol (3).—Sodium borohydride (2.58 g, 0.06 mol) was added to the aldol (1) (4.16 g, 0.02 mol) in methanol (50 ml) at 0 °C and the resultant mixture was stirred for 0.5 h. The excess of borohydride was decomposed by careful addition of ice. Evaporation afforded an oil, which was taken up in ether (100 ml); the solution was washed with saturated brine (5 × 50 ml), dried (Na₂SO₄), filtered, and evaporated to afford the diol (3) (4.17 g, 99%), m.p. 75–78° (from light petroleum-methanol), *m/e* 210 (*M*⁺, 10%), 192 (5), 177 (5), 151 (20), 133 (25), 121 (50), 107 (60), 105 (35), 91 (45), 87 (20), 79 (25), 77 (30), 71 (20), 69 (15), 67 (15), 65 (15), 55 (25), 53 (20), and 45 (100); τ (60 MHz) 9.01 (3 H, s, 6-Me), 8.88 (3 H, s, 6-Me), 8.75 (3 H, d, CH₃-C-OH), 8.14 (3 H, s, 2-Me), 7.91 (2 H, m, ring 5-H₂), 5.85 (1 H, m, CHOH), and 5.3 (d) and 5.1 (d) (1 H, =C-CHOH); 2 isomers in approx. equal amounts); ν_{\max} . 3 400 cm⁻¹ (OH).

Edulans I and II.—(i) *Ion exchange Method.* To the diol (3) (mixture of isomers) (2.05 g, 0.01 mol) in ether (20 ml) was added IR 120 resin (H⁺ form; 5 g) and the mixture was stirred at 20 °C for 3 h. The solution was filtered and evaporated to yield an oil (1.85 g). This was a mixture of three components in the ratio 89 (Y) : 9 (X) : 2 (Z). At 100 °C with a nitrogen flow rate of 40 ml min⁻¹ the retention times after the solvent peak (ether) were X, 7.0; Y, 13.5; Z, 23 min. Pure samples were obtained by preparative g.l.c. (column temperature 150 °C). The main component, Y, was identical (except for optical rotation) with natural edulan I, *trans*-3,5,6,8a-tetrahydro-2,5,5,8a-tetramethyl-2H-1-benzopyran (11); *m/e* 192 (*M*⁺, 7%), 177 (100), 159 (5), 133 (25), 119 (8), 105 (13), 91 (20), 79 (9), 77 (13), 57 (18), 43 (29), and 41 (24); τ (100 MHz) 8.89 (s) and 8.87 (s) (6 H, 5-Me₂), 8.78 (3 H, d, 2-Me, *J* 6 Hz), 8.48 (3 H, s, 8a-Me), 7.98br (4 H, m, 3- and 6-H₂), 5.94 (1 H, m, 2-H), 4.50 (1 H, t, 4-H, *J* 3.8 Hz), and 4.35br (2 H, s, 7- and 8-H) (irradiation at τ 7.98 caused collapse of the triplet at 4.50 to a singlet and the singlet at 4.35br emerged as a broad triplet; irradiation at τ 5.94 produced collapse of the doublet at 8.78 to a singlet); ν_{\max} . (film) 3 030, 2 970, 2 890 (methyl, methylene, methine), 1 447, 1 375 (*gem*-dimethyl), 1 260–1 150 (C–O–C), 1 100, 1 050, 987–1 000, 960–970, 790–840, and 720 cm⁻¹.

The 9% component, X, was identical with natural edulan II, *cis*-3,5,6,8a-tetrahydro-2,5,5,8a-tetramethyl-2H-1-benzopyran (10); *m/e* 192 (*M*⁺, 9%), 177 (100), 159 (15), 133 (36), 119 (17), 105 (19), 91 (26), 79 (12), 71 (17), 55 (14), 43 (34), and 41 (32); τ (100 MHz) 8.84 (6 H, s, 5-Me₂), 8.75 (3 H, d, 2-Me, *J* 4 Hz), 8.59 (3 H, s, 8a-Me), 8.04br (4 H, m, 3- and 6-H₂), 6.57br (1 H, m, 2-H), 4.40br (2 H, s, 7- and 8-H), and 4.26 (1 H, q, 4-H, *J* 4 and 6 Hz) (irradiation

at τ 8.04 caused collapse of the quartet at 4.26 to a broad singlet, and the singlet at 4.40br became a broad doublet; irradiation at τ 6.57 saw collapse of the doublet at 8.75 to a singlet); ν_{\max} . (film) 3 030, 2 970, 2 890 (methyl, methylene, methine), 1 447, 1 375 (*gem*-dimethyl), 1 260–1 150 (C–O–C), 1 075, 960–970, 885, 902, 839, 770, 720, and 690 cm⁻¹.

The 2% component, Z, was not identified but showed *m/e* 192 (*M*⁺, 2%), 177 (6), 133 (9), 129 (38), 121 (16), 105 (14), 91 (14), 71 (18), 59 (100), 43 (42), and 41 (21); τ (100 MHz; CCl₄) 4.41br (s), 9.00 (s), 8.91 (d), 8.73 (s), and 8.71 (s) (12H), 8.27br (s, 4H), 5.90–6.34br (m, 1H), and 4.41br [s superimposed on 4.48br (m)] (3H); ν_{\max} . (film) 3 030, 2 970, 2 980 (methyl, methylene, methine), 1 447, 1 375 (*gem*-dimethyl), 1 260–1 150 (C–O–C), 1 110, 1 050, 987–1 000, 950, 840–790, and 720 cm⁻¹.

(ii) *Boron trifluoride method.* To the diol (3) (mixture of isomers) (100 mg, 0.5 mmol) was added 0.5M-boron trifluoride in ether (10 ml) at 0 °C and the solution was stirred for 30 min. It was then poured into ice-cold saturated aqueous sodium hydrogen carbonate (50 ml) and extracted with ether (3 × 20 ml); the combined extracts were washed with saturated brine (3 × 50 ml), dried (Na₂SO₄), filtered, and evaporated to yield an oil (80 mg). G.l.c. analysis of this residue at 100 and 130 °C showed the presence of two major components, (±)-edulan I (11) and (±)-edulan II (10) in the ratio *ca.* 2 : 7.

Treatment of the diol (3) under the same conditions but for 1 h resulted in an equilibrium mixture of edulans I and II (10 : 1) (g.l.c.).

Isomerisation Experiments.—Treatment of either (±)-edulan I or (±)-edulan II (10 mg) in ether (10 ml) at 20 °C with IR 120 resin (H⁺ form) (0.5 g) for 3–12 h resulted in the equilibrium mixture of (±)-edulans I and II (10 : 1) (g.l.c.).

N.m.r. Experiments.—(i) *Use of shift reagent.* For Y [(±)-edulan I] the quantity used was 38.3 mg in CDCl₃ (0.5 ml) giving a 0.40M-solution. For X [(±)-edulan II] the quantity was 20.1 mg in CDCl₃ (0.5 ml) giving a 0.21M-solution. In these experiments the volume changes on addition of Eu(fod)₃ were ignored, the solutions were not degassed, and although the shift reagent was dried thoroughly before use the solutions were not made up under anhydrous conditions in nitrogen. Thus, the curvature at low shift reagent (L) concentration in a plot of shift against [L]/[S] is attributed to competition between substrate (S) and traces of water and/or acidic impurities for the shift reagent. The curvature at high values of [L]/[S] may be caused by incomplete dissolution of the shift reagent and by medium and association effects. The results are only semi-quantitative but are adequate for the purpose.

Using the expression for single complex formation (L + S \rightleftharpoons LS) and making the usual approximations, we obtain equation (i), where δ = induced chemical shift,

$$\delta = k_B[L]_0\Delta_B / (1 + k_B[S]_0) \quad (i)$$

Δ_B = chemical shift for complex relative to chemical shift for free substrate, [L]₀ = initial concentration of lanthanide, and [S]₀ = initial concentration of substrate. For strong binding or high substrate concentration, $k_B[S]_0 \gg 1$ and $\delta = \Delta_B[L]_0/[S]_0$; thus a plot of δ vs. [L]₀/[S]₀ would give a straight line through the origin of gradient Δ_B . For weak binding or low substrate concentration, $k_B[S]_0 \ll 1$ and $\delta = \Delta_B k_B[L]_0 = k_B \Delta_B [S]_0 ([L]_0/[S]_0)$; thus a plot of δ vs. [L]₀/[S]₀ would be a straight line whose gradient is proportional to [S]₀.

The dependence of induced shifts on the molar ratio of $\text{Eu}(\text{fod})_3$ to substrate is shown in Tables 1—3.

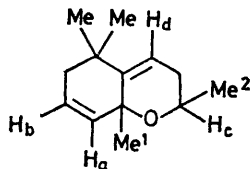


TABLE 1

Chemical shifts (in p.p.m. relative to internal Me_4Si) for compound Y (edulan I)

Spectrum no.	H_a	H_b	H_c	H_d	Me^1	Me^2	$\text{Eu}(\text{fod})_3$ added (mg)	$[\text{L}]_o/[\text{S}]_o$
1	5.65	5.65	4.06	5.50	1.52	1.22	0	0
2	5.65	5.65	4.06	5.50	1.52	1.22	2.1	0.010
3	5.66	5.66	4.07	5.51	1.53	1.23	5.3	0.026
4	5.69	5.67	4.09	5.52	1.54	1.26	12.4	0.060
5	5.76	5.68	4.11	5.53	1.56	1.29	18.7	0.090
6	5.89	5.74	4.18	5.58	1.60	1.37	34.3	0.165
7	6.01	5.77	4.25	5.61	1.64	1.43	50.1	0.241
8	6.10	5.80	4.29	5.65	1.69	1.51	67.7	0.326
9	6.22	5.84	4.36	5.68	1.74	1.58	93.0	0.448
10	6.35	5.89	4.42	5.73	1.80	1.64	116.3	0.560
11	6.43	5.91	4.46	5.75	1.82	1.69	134.6	0.648

(ii) *INDOR and spin decoupling experiments.* Both were carried out on a solution of Y containing $\text{Eu}(\text{fod})_3$ (10 mg) in CDCl_3 . An expansion of the methylene region showed a complex pattern of 16 lines. Irradiation at the resonance line of H_d caused a simplification in the lower field region of the methylene multiplet. Irradiation at the resonance line of H_a and H_b caused a simplification in the higher field region of the methylene multiplet. This shows that the methylene protons at C-3 resonate at lower field than those at C-6.

Each line of the methylene multiplet in an INDOR experi-

TABLE 2

Chemical shifts (in p.p.m. relative to internal Me_4Si) for compound X (edulan II)

Spectrum no.	H_a	H_b	H_c	H_d	Me^1	$\text{Eu}(\text{fod})_3$ added (mg)	$[\text{L}]_o/[\text{S}]_o$
1	5.62	5.58	3.43	5.74	1.41	0	0
2	5.67	5.67	3.45	5.77	1.44	8.4	0.077
3			3.49	5.80	1.51	20.7	0.190
4	5.87	5.69	3.51		1.55	24.7	0.227
5	5.96	5.76	3.52		1.59	30.3	0.275
6	6.20	5.88	3.53		1.66	38.7	0.355
7	6.33	5.99	3.56	5.85	1.73	48.0	0.440
8	6.48	5.98	3.57	5.88	1.78	55.2	0.507
9	6.69	6.09	3.61	5.90	1.88	69.0	0.633
10	6.90	6.18	3.62	5.92	1.97	80.0	0.734

TABLE 3

Comparison of gradients for shifts of protons in substrates X and Y

	Y	X
H_a	1.49	1.70
Me^2	0.86	
H_c	0.73	0.29
Me^1	0.53	0.73
H_b	0.46	0.85
H_d	0.43	0.26

ment was monitored and the effect on the olefinic absorptions was observed. Although the spectrum was complex a qualitative analysis confirmed the assignments already made.

We thank Mrs. J. Street for the 100 MHz spectra, double irradiation, INDOR, and shifted spectra, and Union Carbide U.K. Ltd. for a Research Fellowship (to D. R. A.). We are indebted to Dr. F. B. Whitfield for comparing the synthetic edulans with the natural compounds and for informing us of the results of microhydrogenation.

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