The Synthesis of (±)-10a-Homo-11a-carbathromboxane A₁, a Stable Thromboxane A Analogue

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The thromboxane A₁ (TXA₁) analogue (1), which retains the characteristic bridge oxygen atom of the TXA molecule, has been synthesized from the bicyclic ketone (2). Stereochemical control of alkylation of the bicyclic ketone (2) was achieved by the use of enamines.

Thromboxane A_2 (TXA₂), a metabolite of arachidonic acid, has potent thrombotic and vasoconstrictor properties[1] and is probably involved in the pathogenesis of cardiovascular and other diseases. The instability of the parent substance (half-life ca. 32 s at pH 7.4 and 37 °C) has led to the synthesis of stable analogues[2] which might be used to study the biological properties of compounds of this type. We herein describe full details of our synthesis of a stable thromboxane analogue (1) based on the 8-oxabicyclo[3.2.1]octane ring system.[3]

Although the target compound (1) has a five-membered ring in place of the four-membered ring of TXA₂, a study of models showed that the spatial disposition of the bridge oxygen atom relative to the allylic alcohol and acid functions is essentially the same in the two molecules. The bicyclic structure is considered to be an important requirement for thromboxane A-type activity since the monocyclic thromboxane B_2 (TXB₂) is relatively biologically inactive.

The bicyclic ketone (2) is the starting material for this synthesis. It was envisaged that the activated methylene group at C-2 would permit the attachment of the α-chain by an alkylation-type reaction, the less hindered exo-face of the molecule allowing the alkylation to give the product with the desired exo-stereochemistry. Chain extension from the C-3 carbonyl group would then enable the β-side-chain to be built up. Published methods[4-6] for the synthesis of the ketone (2) or its unsaturated precursor (3) involve the cycloaddition of various oxyallyl cations to furan. However, the procedures described[4,5] are only for small-scale preparations utilising costly reagents. A larger scale synthesis of the ketone (2) has thus been developed, utilising the triethyl borate–zinc method of Hoffmann and Iqbal[6] to generate a bromo-oxyallyl cation from 1,1,3,3-tetrabromopropanone. Debromination of the resultant bromo ketones (4a and b) with a zinc–copper couple

and subsequent catalytic hydrogenation gave the ketone (2) in 52% overall yield from 1,1,3,3-tetrabromopropanone (47% from propanone).
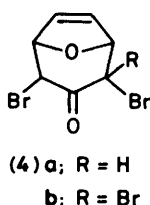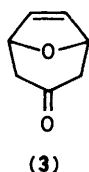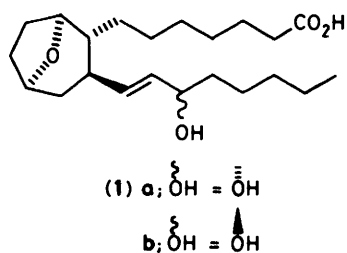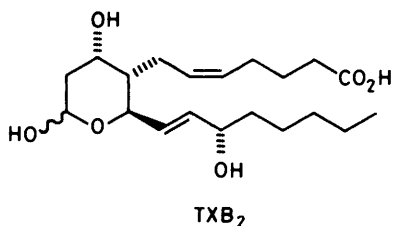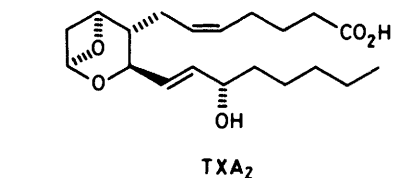
Alkylation of the crystalline pyrrolidine enamine (5) of the ketone (2) with the tetrahydropyranyl (THP) ether of 7-bromoheptanol gave exclusively the desired exo-alkylated product (6) (Scheme 1). The product was shown to be a single isomer with exo-orientation of the alkyl chain by n.m.r. spectroscopy and X-ray crystallography, as discussed below. The use of enamines was prompted by unsuccessful attempts to effect direct alkylation of the ketone (2), probably a consequence of difficulty in forming the enolate anion. The pyrrolidine enamine (5) was also alkylated with the methyl ester of 7-bromoheptanoic acid to form exclusively the exo-alkylated product (7). The X-ray crystal structure[7] of (7) confirmed that the alkyl chain had the exo-orientation.

The yield of product obtained from the enamine–alkyl halide reaction was very dependent upon the individual alkyl halide, the reaction conditions (Table 1), and the enamine base. The best yields were obtained using the pyrrolidine enamine (5) and an alkyl bromide in dioxane at 80 °C, the morpholine enamine (8) giving consistently lower yields.

The morpholine enamine (8) was also condensed with the aldehyde ester (9) to give the enone ester (10) (Scheme 2). Catalytic hydrogenation of the enone (10) gave exclusively the endo-alkylated ketone (11), hydrogenation proceeding by addition of hydrogen from the less hindered face of the molecule (10). A comparison of the ¹H n.m.r. spectra of the exo- (7) and the endo- (11) alkylated ketones permitted an unambiguous assignment of the stereochemistry of each of the alkylation products and an evaluation of their isomeric purity. The signals for the individual bridgehead protons (H_A and H_B) and for the exo-proton(s) adjacent to the keto group [H_D (H_C)]
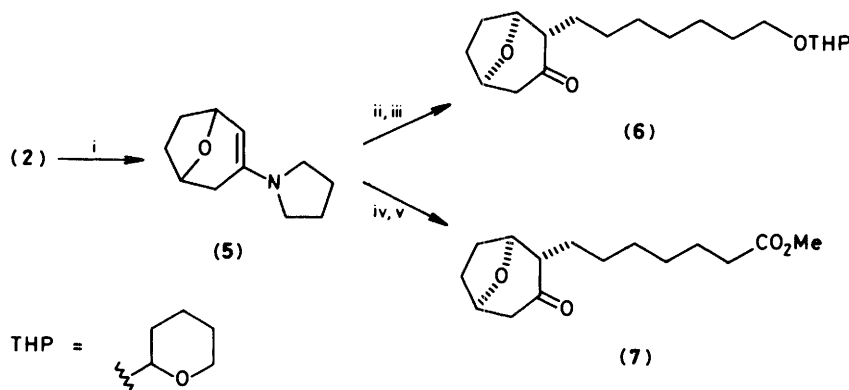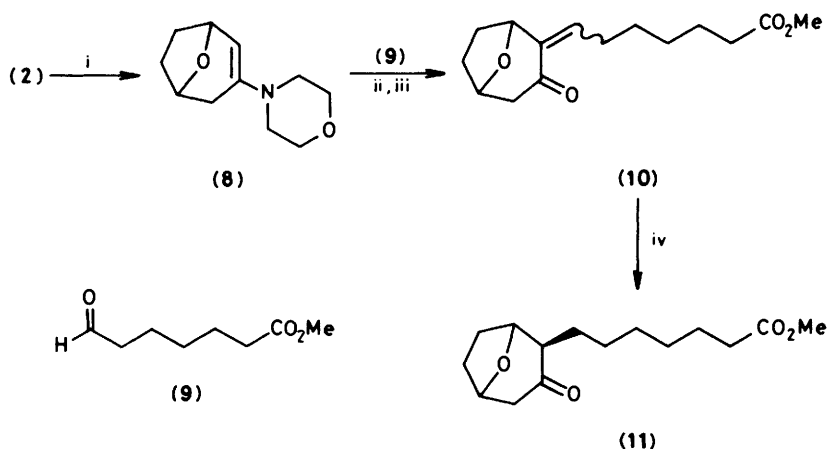

Scheme 1. Reagents: i, pyrrolidine, −H₂O; ii, Br[CH₂]₇OTHP, dioxane; iii, H₂O; iv, Br[CH₂]₆CO₂Me, dioxane; v, H₃O⁺

TXA₂

TXB₂

(1) a; $\overset{\wr}{O}H$ = $\overset{\equiv}{O}H$

b; $\overset{\wr}{O}H$ = $\overset{\uparrow}{O}H$

(2)   (3)   (4) a; R = H

                          b; R = Br

were clearly separated on the n.m.r. spectra and are characteristic for each of the isomers, as outlined in Table 2.

It was envisaged that the keto THP ether (6) would undergo homologation to the aldehyde (17) *via* a Wittig condensation with (methoxymethylene)triphenylphosphorane. However, the keto THP ether (6) would not react with either the methoxymethylenephosphorane [from (methoxymethyl)triphenylphosphonium chloride and butyl-lithium: (i) tetrahydrofuran (THF), 25 °C, 40 h or (ii) THF–diglyme, 25 °C, 20 h then diglyme 160 °C, 8 h] or the methylenephosphorane [from methyltriphenylphosphonium bromide and butyl-lithium:

Table 1. The enamine–alkyl halide reaction for the pyrrolidine enamine (3)

Alkyl halide	Conditions (dioxane solvent)	Yield of (6) or (7)
Br[CH₂]₇OTHP	80—85 °C, 70 h	16% (6)
	Reflux, 23 h	0% (6)
Br[CH₂]₆CO₂Me	65—80 °C, 17 h then	18% (7)
	100 °C, 1 h	18% (7)
	100 °C, 18 h	10% (7)
	100 °C, 36 h	6% (7)
	100 °C, 10 h	5% (7)
I[CH₂]₆CO₂Me	100 °C, 18 h	6% (7)

Table 2. The characteristic ^1H n.m.r. signals of the *exo*-(6)/(7) and *endo*-(11) alkylated ketones

	N.m.r. signal for	
Proton	*exo*-alkylated ketone (6)/(7)	*endo*-alkylated ketone (11)
H_A	br d, J 6 Hz, δ 4.43	br t, J 6 Hz, δ 4.54
H_B	br t, J 5 Hz, δ 4.65	br t, J 5 Hz, δ 4.70
H_C		complex 2 H δ 2.50—2.82
H_D	d of d, 1 H J 16 and 5 Hz, δ 2.77	

THF, 25 °C, 40 h] to form an alkene. This was probably for steric reasons since the unsubstituted ketone (2) readily underwent these Wittig reactions to give the alkenes (12a) and (12b) respectively. The reaction of the keto ester (7) with these Wittig reagents was also investigated, but no alkene product was detected and a reaction with the ester function occurred when forcing conditions were used. Alternative methods for the homologation to the aldehyde (17) were thus investigated using the keto THP ether (6).

(12) a ; R = OMe

b ; R = H

(13)

Scheme 2. *Reagents:* i, morpholine, −H₂O; ii, toluene; iii, H₃O⁺; iv, H₂, 10% Pd–C

The less bulky *N*-methylphenylsulphonimidoylmethyl-lithium reagent[8] (13) reacts with the keto THP ether (6) to afford the β-hydroxysulphoximides (14), which yielded the alkene THP ether (15) upon reductive elimination with aluminium amalgam and aqueous acetic acid in THF (Scheme 3). The synthesis was best carried out without purification of the intermediate β-hydroxysulphoximides (14), whereupon a 66% yield of the alkene (15) was obtained from the ketone (6). The diastereoisomers of (14) were, however, separated by chromatography, whereupon the reductive elimination of each isomer to the alkene (15) was found to be quantitative. Use of di-iodomethane and magnesium amalgam,[9] a possible one-step reaction for the transformation (6) ⟶ (15), failed with (6), again probably for steric reasons since the expected product (12a) was readily formed from the unsubstituted ketone (2).

Hydration of the alkene THP ether (15) by treatment with borane–THF complex followed by alkaline hydrogen peroxide gave the hydroxy THP ether (16). It was anticipated that the *cis*-(*exo*-2, *exo*-3)-isomer of (16) would predominate since hydroboration normally proceeds by an anti-Markovnikov *cis*-addition from the less hindered side of the molecule, and the *endo*-face of (15) was considered to have least steric hindrance; the *exo*-alkyl group adjacent to the carbonyl group was expected to render greater steric hindrance to the *exo*-face than the ethano bridge to the *endo*-face. Upon oxidation with pyridinium chlorochromate in sodium acetate-buffered dichloromethane the hydroxy THP ether (16), which appeared homogeneous by t.l.c., gave an 8:3 mixture (distinguished and estimated by ¹H n.m.r. spectroscopy) of the aldehydes (17) and (18). The *cis*-isomer (17) was expected to be the major product, and the *trans*-isomer (18) to be the thermodynamically more stable product. Indeed, treatment of the 8:3 mixture of aldehydes (17) and (18) with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in dichloromethane transformed it into a 3:7 mixture,
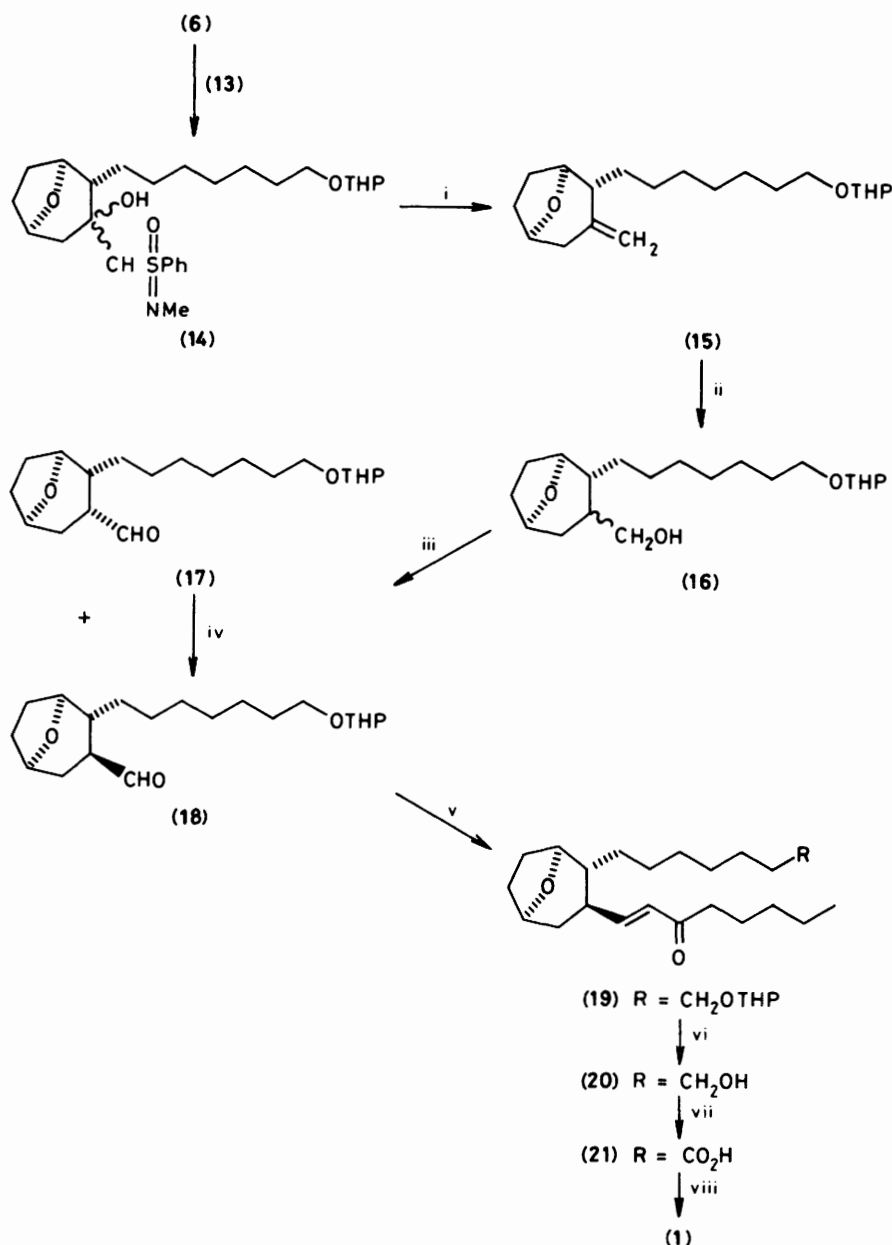

Scheme 3. *Reagents:* i, Al–Hg, aq.HOAc, THF; ii, BH₃–THF; iii, pyridinium chlorochromate, NaOAc, CH₂Cl₂; iv, DBN, CH₂Cl₂ then chromatography; v, (MeO)₂PO·CHNa·CO·C₅H₁₁, THF; vi, H₃O⁺, EtOH; vii, pyridinium dichromate; viii, LiBuˢ₃BH, THF

presumably in favour of the *trans*-isomer (18). No further
isomerisation could be induced, under strong basic or acidic
conditions, probably because of the non-coplanarity of the *cis*-
substituents in the bicyclic ring and the steric hindrance of the
ethano bridge to the *endo*-face of the molecule. The aldehydes
(17) and (18) were separated by pressure column chrom-
atography (l.p.l.c.) using t.l.c. silica gel and the *trans*-aldehyde
(18) was treated with the sodio derivative of dimethyl 2-
oxoheptylphosphonate to give the enone THP ether (19). The
C-3 epimeric relationship of the two aldehydes was shown by
treating the chromatographically separated *cis*-aldehyde (17)
with DBN to give a similar 3:7 mixture of *cis*-(17) and *trans*-
(18) aldehydes as before. The ^{1}H n.m.r. spectrum of the *trans*-
aldehyde (18) showed the characteristic deshielded *exo*-proton
adjacent to the formyl group.

Acid-catalysed cleavage of the THP ether protecting group of
the enone (19) gave the enone alcohol (20) which was oxidised
by pyridinium dichromate in dimethylformamide (DMF) to the
enone acid (21). The synthesis was then completed by reduction
of the latter with lithium tri-s-butylborohydride (L-
Selectride) in THF at 0 °C to give the TXA$_1$ analogue (1) as a
mixture of diastereomeric alcohols (1a and b).

(22)
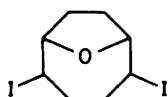
(23)   (24)

An alternative route to these thromboxane analogues *via* the
aldehyde synthon (31) was also investigated. Conjugate
addition of an organo-copper reagent [*e.g.* (22)] to (31) was
expected to yield a product with the required stereochemistry at
C-2 and C-3 for the side-chains. A mixture of 9-oxabicyclo-
[4.3.1.]non-2-ene (25) and -3-ene (26) was prepared by the
method of Cope *et al.*[10] from cyclo-octa-*cis*-1,*cis*-5-diene *via* the
di-iodide (23) and the diene (24). However, olefinic cleavage of
alkenes (25) and (26) by reductive ozonolysis or with osmium
tetraoxide and sodium metaperiodate failed, presumably due to
the instability of the resultant dialdehydes (29) and (30).
Nevertheless, hydroxylation of the alkenes (25) and (26) by the
hydrogen peroxide-formic acid method[11] and oxidative
cleavage of the resultant diols (27) and (28) with sodium
metaperiodate (0.25 h), followed immediately by an *in situ*

intramolecular aldol condensation by basification with aqueous
potassium hydroxide, gave a mixture (1:1) of the desired
aldehyde (31) and its isomer (32) in low yield (Scheme 4). The
route was not further investigated owing to difficulties in
preparative separation of the cyclised aldehydes (31) and (32)
and their precursors.

The thromboxane A$_1$ analogue [mixture of diastereoisomers
(1a) and (1b)] showed weak thromboxane A$_2$-like properties
with respect to vasoconstriction on rabbit arterial tissue, but no
pro-aggregatory or antagonistic effects on human platelets at
concentrations up to 100μM.

Experimental

(25)   (27)   (29)   (31)

 +   ⟶i   +   ⟶ii   +   ⟶iii   +

(26)   (28)   (30)   (32)

Scheme 4. *Reagents:* i, H$_2$O$_2$, HCO$_2$H then steam distillation; ii, aq.NaIO$_4$; iii, 0.5M aq.KOH

ground calcium hydride or 4 Å molecular sieves. Light petroleum refers to the fraction with boiling range 40—60 °C, ether to diethyl ether, dioxane to 1,4-dioxane, and Cardice to solid CO_2 throughout.

8-*Oxabicyclo*[3.2.1]*oct-6-en-3-one*[4] (3).—A solution of 1,1,3,3-tetrabromopropanone (374 g, 1.0 mol), prepared by the acid-catalysed tetrabromination of acetone,[12] and triethyl borate (200 ml, 172 g, 1.2 mol) in dry THF (200 ml) was added during 1.5 h to a mixture of zinc powder (68.6 g, 1.05 g-atom) and dry furan (136 g, 2.0 mol) in dry THF (200 ml) stirred under nitrogen and protected from light. The ensuing reaction heated the mixture to reflux, and the mixture was stirred overnight (19 h) at room temperature. The mixture was then cooled to −15 °C, treated with water (200 ml), and stirred at 0 °C for 0.3 h. Insoluble material was filtered off and washed with ether (500 ml) and the combined filtrates were diluted with water (800 ml). The heavy organic layer was separated, and the aqueous layer was extracted with ether (2 × 350 ml) which had first been used to wash further the insoluble material. The combined organic layers were washed with saturated aqueous sodium chloride, dried, and concentrated at *ca.* 30 °C. The residue was treated with methanol (200 ml) and immediately added to a stirred and cooled (Cardice–acetone bath) mixture of powdered zinc-copper couple[13] [from Zn 230 g, 3.5 g-atom)] and ammonium chloride (250 g) in methanol (1 l) at a rate such that the internal temperature was maintained at 15—25 °C. The mixture was stirred overnight at room temperature under nitrogen and protected from light, and was then filtered. The solid was washed with dichloromethane (900 ml) and the combined filtrates were diluted with water (1.6 l), the organic layer was separated, and the aqueous layer was extracted with dichloromethane (300 ml + 4 × 150 ml). The combined organic layers were dried and the solvent was removed by distillation, initially at atmospheric pressure and then under reduced pressure; direct distillation (no condenser) *in vacuo* of the magnetically stirred residue (from a flask heated in a hot-water bath up to 100 °C) into a cooled (Cardice–acetone) flask gave the ketone (3) (67.1 g, 54%) (distillation temperature *ca.* 40—80 °C at 0.3 mmHg) as a white crystalline solid, m.p. 38—39 °C (lit.,[4] 38 °C). The product was stored in the dark at −20 °C under argon. The preparation also proceeds satisfactorily at twice the above scale, to give a similar percentage yield of the ketone (3).

8-*Oxabicyclo*[3.2.1]*octan-3-one*[4] (2).—Hydrogenation of the unsaturated ketone (3) [10% palladium–carbon catalyst (5% w/w), ethyl acetate solvent] for 2 h at room temperature followed by distillation into a cooled (Cardice–acetone) flask gave the ketone (2) (95%), b.p. 43—44 °C at 0.05 mmHg, as a white crystalline solid which melted upon being warmed to room temperature; δ (100 MHz) 4.71 (2 H, br m, 1- and 5-H), 2.71 (2 H, dd, J 16 and 5 Hz, 2-H_{exo} and 4-H_{exo}), 2.27 (2 H, d, J 5 Hz, 2-H_{endo} and 4-H_{endo}), and 2.2—1.6 (4 H, m, 6- and 7-H).

3-*Pyrrolidinyl-8-oxabicyclo*[3.2.1]*oct-2-ene* (5).—A mixture of the ketone (2) (18.9 g, 0.15 mol) and dry pyrrolidine (11.7 g, 0.165 mol) in dry benzene (90 ml) was heated under nitrogen for 20 h under a Soxhlet extractor containing calcium hydride (15 g). The mixture was then concentrated and distilled (short-path) to give the *pyrrolidine enamine* (5) (21.7 g, 81%) as a pale yellow oil, b.p. 70—90 °C at 0.05 mmHg, which solidified, on being cooled, to a light yellow crystalline solid, m.p. 44—49 °C (Found: M^+, 179.1313. $C_{11}H_{17}NO$ requires M, 179.1310); $\lambda_{max.}$ 248 nm; $\nu_{max.}$ 3 050 (H–C=C) and 1 630 cm^{-1} (C=C); δ (100 MHz) 4.51 (2 H, br m, 1- and 5-H), 4.37 (1 H, d, J 5 Hz, C=C–*H*), 2.98 (4 H, m, CH_2NCH_2), 2.68 (1 H, dd, J 5 and 12 Hz, 4-H_{exo}), and 2.4—1.6 (9 H, complex m, 4-H_{endo}, 6- and 7-H_2, and 2 × NCH_2CH_2).

The enamine was stored under argon at −20 °C.

exo-2-[7-(*Tetrahydropyran-2-yloxy*)*heptyl*]-8-*oxabicyclo*-[3.2.1]*octan-3-one* (6).—A mixture of the pyrrolidine enamine (5) (10.0 g, 0.056 mol) and 1-bromo-7-(tetrahydropyran-2-yl)heptane[14] (16.2 g, 0.058 mol) in dry dioxane (30 ml) was stirred under nitrogen and heated at 80—85 °C for 70 h. Water (3 ml) was then added and the mixture was stirred for a further 0.7 h at 80 °C. The cooled solution was diluted with water (300 ml), extracted with ether (100 ml), saturated with sodium chloride, and then further extracted with ether (3 × 100 ml). The combined extracts were washed successively with water and saturated aqueous sodium chloride, dried, and concentrated. The residual oil (13.7 g) was purified l.p.l.c. (Kieselgel 60 H, 500 g) [ether–light petroleum (1:1) as eluant] to give the exo-*keto THP ether* (6) (2.85 g, 16%) as an oil which crystallised after a considerable time, m.p. 38—42 °C (Found: C, 70.0; H, 10.1%; M^+, 324.2308. $C_{19}H_{32}O_4$ requires C, 70.3; H, 9.9%; M, 324.2301); t.l.c. one component, R_F 0.20 [ether–light petroleum (1:1)]; $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ (100 MHz) 4.65 (1 H, br t, J 5 Hz, 5-H), 4.56 [1 H, br s, OC(H)O], 4.43 (1 H, br d, J 6 Hz, 1-H), 4.00—3.26 (4 H, complex m, 2 × OCH_2), 2.77 (1 H, dd, J 16 and 5 Hz, 4-H_{exo}), and 2.32—1.23 (24 H, complex m, 2-H_{endo}, 4-H_{endo} 6- and 7-H_2, and 9 × CH_2).

Methyl 7-(3-*Oxo-8-oxabicyclo*[3.2.1]*octan-exo-2-yl*)*heptanoate* (7).—A mixture of the pyrrolidine enamine (5) (6.6 g, 37 mmol) and methyl 7-bromoheptanoate[15] (16.4 g, 74 mmol), prepared by the acid-catalysed esterification of 7-bromohep-tanoic acid,[16] in dry dioxane (20 ml) was heated under nitrogen on a steam-bath for 18 h [gently (*ca.* 80 °C reaction temperature) for 16 h and vigorously for 2 h]. Water (5 ml) was then added, and the mixture was heated for a further 1 h on the steam-bath. The cooled mixture was diluted with water (200 ml), acidified with dilute hydrochloric acid (2M; 5 ml), and extracted with ether (80 ml). The aqueous layer was then saturated with sodium chloride and further extracted with ether (3 × 80 ml). The combined extracts were dried, concentrated, and distilled (short-path) to give the exo-*keto ester* (7) (1.75 g, 18%) as a pale yellow oil, b.p. 120—170 °C at 0.05 mmHg, which crystallised on being cooled, m.p. 50—54 °C (Found: C, 66.9; H, 9.0%; M^+, 268.1671. $C_{15}H_{24}O_4$ requires C, 67.1; H, 9.0%; M, 268.1675); t.l.c. one component, R_F 0.36 [ether–light petroleum (4:1)]; $\nu_{max.}$ 1 735 (C=O, ester) and 1 710 cm^{-1} (C=O, ketone); δ (100 MHz) 4.65 (1 H, br t, J 5 Hz, 5-H), 4.43 (1 H, br d, J 6 Hz, 1-H), 3.65 (3 H, s, CO_2Me), 2.77 (1 H, dd, J 16 and 5 Hz, 4-H_{exo}), and 2.4—1.2 (18 H, complex m, 2-H_{endo}, 4-H_{endo}, 6- and 7-H_2, and [CH_2]$_6$).

3-*Morpholino-8-oxabicyclo*[3.2.1]*oct-2-ene* (8).—A mixture of the ketone (2) (11.5 g, 0.09 mol) and dry morpholine (25.0 g, 0.29 mol) in dry toluene (80 ml) was heated under nitrogen under a Soxhlet extractor containing calcium hydride for 42 h. The mixture was then concentrated and distilled (short-path) to yield the *morpholine enamine* (8) (14.6 g, 82%) as a pale yellow oil, b.p. 70—90 °C at 0.02 mmHg, which solidified on being cooled to give a pale yellow crystalline solid, m.p. 51—55 °C (Found: M^+, 195.1260. $C_{11}H_{17}NO_2$ requires M, 195.1259); $\lambda_{max.}$ 245 nm; $\nu_{max.}$ 3 060 (H–C=C) and 1 635 cm^{-1} (C=C); δ (100 MHz) 4.79 (1 H, d, J 5 Hz, C=C–H), 4.56 (2 H, br m, 1- and 5-H), 3.70 (4 H, t, J 5 Hz, CH_2OCH_2), 3.0—2.6 (5 H, br m, CH_2NCH_2 and 4-H_{exo}), and 2.3—1.6 (5 H, complex m, 4-H_{endo}, and 6- and 7-H_2).

Methyl 7-(3-*Oxo-8-oxabicyclo*[3.2.1]*octan-2-ylidene*)*hep-tanoate* (10).—A mixture of the morpholine enamine (8) (0.40 g,

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* Unprimed locants refer to oxabicyclo-octa(e)ne ring.

2.0 mmol) and methyl 7-oxoheptanoate [17] (9) (0.32 g, 2.0 mmol) in dry toluene (5 ml) was heated under reflux under nitrogen. A Soxhlet extraction thimble containing calcium hydride was placed in the path of the condensing vapours in order to remove the water formed during the reaction. Extra portions of the aldehyde ester (9) (0.16 g, 1.0 mmol) dissolved in dry toluene (1 ml) were added to the mixture after 20, 40, and 60 h. After 74 h at reflux the mixture was cooled to 0 °C and treated dropwise with, in turn, concentrated hydrochloric acid (0.2 ml) and then water (0.2 ml). The resultant mixture was stirred at room temperature for 1 h and then diluted with water (3 ml) and stirred for a further 0.5 h. The organic layer was then separated, the aqueous layer was extracted with ether (3 × 3 ml), and the combined organic layers were then washed successively with saturated aqueous sodium hydrogen carbonate and saturated aqueous sodium chloride, dried, and concentrated. The residual oil was distilled (short-path) and the high boiling fraction (b.p. 100—200 °C at 0.03 mmHg) was subjected to p.l.c. [ether–light petroleum (4 : 1)] to give the *enone ester* (10) (0.085 g, 16%) as an oil (Found: M^+, 266.1509. $C_{15}H_{22}O_4$ requires M, 266.1518); t.l.c. one component, R_F 0.30 [ether–light petroleum (4 : 1)]; $\lambda_{max.}$ 243 nm (ε 6 000 dm³ mol⁻¹ cm⁻¹); $\nu_{max.}$ 1 695 (C=O) and 1 625 cm⁻¹ (C=C); δ* (80 MHz) 6.55 (1 H, td, J 8 and 1 Hz, C=C–H), 5.17 (1 H, br d, J 5 Hz, 1-H), 4.69 (1H, br t, J 6 Hz, 5-H), 3.65 (3 H, s, CO_2Me), 2.78 (1 H, dd, J 18 and 6 Hz, 4-H_{exo}), and 2.45—1.15 (15 H, complex m, 4-H_{endo}, 6- and 7-H_2, and $[CH_2]_5$).

Methyl 7-(3-Oxo-8-oxabicyclo[3.2.1]octan-endo-2-yl)heptano-ate (11).—Hydrogenation of the enone ester (10) [10% palladium–carbon catalyst (25% w/w), methyl acetate solvent] for 0.2 h at 18 °C gave the endo-*keto ester* (11) (99%) as an oil (Found: M^+, 268.1676. $C_{15}H_{24}O_4$ requires M, 268.1675); t.l.c. one component, R_F 0.37 [ether–light petroleum (4 : 1)]; $\nu_{max.}$ 1 735 (C=O, ester) and 1 710 cm⁻¹ (C=O, ketone); δ* (100 MHz) 4.70 (1 H, br t, J 5 Hz, 5-H), 4.54 (1 H, br t, J 6 Hz, 1-H), 3.65 (3 H, s, CO_2Me), 2.82—2.50 (2 H, m, 2-H_{exo} and 4-H_{exo}), and 2.42—1.24 (17 H, complex m, 4-H_{endo}, 6- and 7-H_2, and [CH₂]₅).

3-Methoxymethylene-8-oxabicyclo[3.2.1]octane (12a).—A solution of butyl-lithium (1.6M; 5.0 ml, 8.0 mmol) in hexane was added dropwise to an ice-cooled and magnetically stirred suspension of (methoxymethyl)triphenylphosphonium chloride (2.74 g, 8.0 mmol) in dry THF (10 ml) under argon, and the resultant deep red solution of the phosphorane was allowed to warm to 15 °C during 0.7 h. A solution of the ketone (2) (0.50 g, 4.0 mmol) in dry THF (1 ml) was then added and the mixture was stirred at room temperature (25 °C) for 20 h and then concentrated at 30 °C to remove most of the THF. The residue was partitioned between water and ether, and the combined ethereal extracts were dried and concentrated at 30 °C. The residue was triturated with pentane, the crystals of triphenyl-phosphine oxide were filtered off, and the pentane solution was concentrated at 30 °C and then distilled (short-path) to give the *methoxyvinyl compound* (12a) (0.41 g, 67%) as a liquid, b.p. 65—75 °C at 14 mmHg; t.l.c. one component, R_F 0.43 [ether–light petroleum (2 : 1)]; $\nu_{max.}$ 1 680 cm⁻¹ (C=C); δ (80 MHz) 5.86 (1 H, t, J 2 Hz, CHOMe), 4.41 (2 H, br s, 1- and 5-H), 3.55 (3 H, s, OMe), 2.44 (2 H, d of br m, J 14 Hz, 2-H_{exo} and 4-H_{exo}), and 2.25—1.45 (6 H, complex m, 2-H_{endo}, 4-H_{endo}, and 6-and 7-H_2).

3-Methylene-8-oxabicyclo[3.2.1]octane (12b).—Using the method described for the preparation of compound (12a), the ketone (2) was treated with the phosphorane generated from methyltriphenylphosphonium chloride. The organic solutions were carefully concentrated at atmospheric pressure and the residue was distilled (short-path) to afford the *alkene* (12b) (54%) as a volatile liquid, b.p. 130—150 °C; t.l.c. one component, R_F 0.51 [ether–light petroleum (2 : 1)]; $\nu_{max.}$ 1 645 cm⁻¹ (C=C); δ (60 MHz) 4.75 (2 H, br t, J 2 Hz, C=CH₂), 4.4 (2 H, br s, 1- and 5-H), 2.5 (2 H, d of br s, J 15 Hz, 2-H_{exo} and 4-H_{exo}), and 2.1—1.5 (6 H, complex m, 2-H_{endo}, 4-H_{endo}, and 6- and 7-H_2).

3-[(N-Methylphenylsulphonimidoyl)methyl]-exo-2-[7-(tetra-hydropyran-2-yloxy)heptyl]-8-oxabicyclo[3.2.1]octan-3-ol (14).—A solution of butyl-lithium (1.1M; 3.8 ml, 4.2 mmol) in hexane was slowly added dropwise to a stirred solution of N,S-dimethyl-S-phenylsulphoximide[8] (0.73 g, 4.3 mmol) in dry THF (12 ml) maintained at 0 °C under argon. The mixture was stirred for 1 h at 0 °C, and then treated with a solution of compound (6) (1.0 g, 3.1 mmol) in dry THF (2 ml) and stirred for a further 1 h at 0 °C and for 5 h at room temperature. The solution was then diluted with cold aqueous ammonium chloride (10%; 60 ml) and extracted with ether, and the combined extracts were washed with aqueous sodium chloride (20%, then saturated), dried, and concentrated to afford the crude β-*hydroxy sulphoximides* (14) (1.6 g) (ca. 70% yield from n.m.r. spectrum). P.l.c. (ether) on an analytical sample of the product separated the diastereoisomers (C-3 epimers) to afford isomer A (Found: M^+, 493.2880. $C_{27}H_{43}NO_5S$ requires M, 493.2862); t.l.c. one component, R_F 0.31 (ether); $\nu_{max.}$ 3 270 (O–H) and 1 235 and 1 145 cm⁻¹ (O=S=N); δ* (100 MHz) 7.87 and 7.61 (together 5 H, 2 × m, ArH), 4.56 (1 H, br s, O–CH–O), 4.42 (1 H, br m, 5-H), 4.25 (1 H, br d, 1-H), 4.06—3.34 [6 H, complex, 2 × OCH₂ and CH_2S(O)=NMe], 2.61 (3 H, s, NMe), and 2.56—1.26 (26 H, complex, 2-H, 4-, 6-, and 7-H₂, 9 × CH₂, and OH) and isomer B (Found: M^+, 493); t.l.c. one component, R_F 0.24 (ether); $\nu_{max.}$ 3 270 (O–H) and 1 235 and 1 145 cm⁻¹ (O=S=N); δ* (100 MHz) 7.87 and 7.61 (together 5 H, 2 × m, ArH, 4.56 (1 H, br s, O–CH–O), 4.46—4.20 (2 H, br complex m, 1- and 5-H), 4.0—3.32 [6 H, complex, 2 × OCH₂ and CH₂S(O)=NMe], 260 (3 H, s, NMe), and 2.55—1.25 [26 H, complex, 2-H, 4-H_{exo} (δ 2.27, dd, J 14 and 5 Hz), 4-H_{endo}, 6- and 7-H₂, 9 × CH₂, and OH].

3-Methylene-exo-2-[7-(tetrahydropyran-2-yloxy)heptyl]-8-oxabicyclo[3.2.1]octane (15).—Aluminium turnings (16 g, 0.59 g-atom) were etched with aqueous sodium hydroxide (2M), washed superficially with water, and then stirred for 120 s with aqueous mercury(II) chloride (2%; 200 ml). The process was repeated and the resultant amalgam was washed successively with water, ethanol, and ether and immediately added to a stirred and cooled (cold-water bath at 15 °C) solution of the crude β-hydroxy sulphoximides (14) [1.6 g; from (6) 1.0 g, 3.1 mmol] in THF (160 ml) to which a mixture of acetic acid–water (1 : 1; 80 ml) had been added. The mixture was stirred for 5 h at 15—25 °C and then diluted with water (1.5 l) and extracted with ether (4 × 300 ml). The combined extracts were washed successively with aqueous sodium hydroxide (20%; 2 × 200 ml) and aqueous sodium chloride (20%), dried, and concentrated. The residual oil (1.1 g) was purified by l.p.l.c. (Kieselgel 60 H, 110 g) [ether–light petroleum (1 : 1) as eluant] to afford the *alkene-THP ether* (15) [0.66 g, 66% from (6)] (Found: M^+, 322.2513. $C_{20}H_{34}O_3$ requires M, 322.2508); t.l.c. one component, R_F 0.49 [ether–light petroleum (1 : 1)]; $\nu_{max.}$ 3 070 (C=C) and 1 645 cm⁻¹ (C=C); δ* (80 MHz) 4.75 (2 H, m, C=CH₂), 4.56 (1 H, br s, O–CH–O), 4.40 (1 H, br m, 5-H), 4.22 (1 H, br d, J 5 Hz, 1-H), 4.0—3.2 (4 H, complex m, 2 × OCH₂), 2.57 (1 H, d of br s, J 15 Hz, 4-H_{exo}), and 2.1—1.1 (24 H, complex, 2-H, 4-H_{endo}, 6- and 7-H₂, and 9 × CH₂) and unchanged ketone (6) (0.18 g recovery).

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* Unprimed locants refer to oxabicyclo-octa(e)ne ring.

3-*Hydroxymethyl*-exo-2-[7-(*tetrahydropyran-2-yloxy*)-*heptyl*]-8-*oxabicyclo*[3.2.1]*octane* (**16**).—A solution of borane–THF complex (0.83M; 2.0 ml, 1.7 mmol) in THF was slowly added dropwise to a stirred solution of the alkene (**15**) (0.40 g, 1.2 mmol) in dry THF (5 ml) maintained at 0 °C under argon. The resultant solution was stirred at room temperature for 2.5 h and then cautiously treated successively with water (0.2 ml), aqueous sodium hydroxide (3M; 0.6 ml), and aqueous hydrogen peroxide (30%; 0.6 ml) (reaction temperature 30—35 °C) and heated at 45—50 °C for 1 h. The cooled mixture was diluted with ether (8 ml) and water (3 ml), the organic layer was separated, and the aqueous layer was extracted with ether (2 × 3 ml). The combined organic layers were washed successively with water and saturated aqueous sodium chloride, dried (K_2CO_3, $MgSO_4$), and concentrated to afford the *hydroxy-THP ether* (**16**) (0.42 g, 99%), sufficiently pure to proceed with the next stage. An analytical sample was purified by p.l.c. (ether) (Found: M^+, 340.2617. $C_{20}H_{36}O_4$ requires M, 340.2614); t.l.c. one component, R_F 0.26 (ether); $v_{max.}$ 3 440 cm^{-1} (O–H); δ * (80 MHz) 4.56 (1 H, br s, O–CH–O), 4.31 (1 H, br m, 5-H), 4.15 (1 H, br d, J 6 Hz, 1-H), 4.2—3.2 [6 H, complex, 2 × OCH_2 and CH_2OH (δ 3.63, d, J 7 Hz)], and 2.3—1.0 (27 H, complex, 2- and 3-H, 4-, 6-, and 7-H_2, 9 × CH_2, and OH).

cis- *and* trans-3-*Formyl*-exo-2-[7-(*tetrahydropyran-2-yloxy*)-*heptyl*]-8-*oxabicyclo*[3.2.1]*octane* (**17**) *and* (**18**).—A solution of the alcohol (**16**) (0.20 g, 0.59 mmol) in dry dichloromethane (0.8 ml) was added in one portion to a vigorously stirred suspension of pyridinium chlorochromate (0.26 g, 1.2 mmol) in dry dichloromethane (2 ml) containing anhydrous sodium acetate (22 mg, 0.27 mmol), and the resultant mixture was stirred under argon at room temperature for 1.8 h. Dry ether (10 ml) was then added, the supernatant liquid was decanted, and the insoluble residue was washed thoroughly with dry ether (3 × 5 ml) to leave a granular solid. The combined organic layers were filtered through a short column of anhydrous magnesium sulphate and then concentrated to afford the aldehydes (**17**) and (**18**) (0.18 g, 91%); δ (80 MHz) 9.80 (A) and 9.65 (B) [together 1 H, 2 × s, 2 × CHO, (A):(B) 8:3]; t.l.c. R_F 0.38 (A) and 0.34 (B) [acetone–light petroleum (1:5)], intensity (A)>(B). cis-trans Isomerisation of the aldehydes (**17**) and (**18**) was effected by refluxing the mixture (0.18 g) under argon with a solution of DBN (0.1M; 2.5 ml) in dry dichloromethane for 2.5 h. The cooled mixture was diluted with dry ether (15 ml), filtered through a short column of silica gel, and then concentrated to afford the aldehydes (**17**) and (**18**) (0.16 g, 99% recovery); δ (80 MHz) 9.80 (A) and 9.65 (B) [together 1 H, 2 × s, 2 × CHO, (A):(B) 3:7]; t.l.c. R_F 0.38 (A) and 0.34 (B) [acetone–light petroleum (1:5)] intensity (B)>(A). The mixture was separated by l.p.l.c. (Kieselgel 60 H, 30 g) [acetone–light petroleum (1:25) as eluant] to give the cis-*aldehyde* (**17**) [30 mg, 15% from (**16**)] (Found: M^+, 338.2464. $C_{20}H_{34}O_3$ requires M, 338.2457); t.l.c. one component, R_F 0.38 [acetone–light petroleum (1:5)]; $v_{max.}$ 1 725 cm^{-1} (C=O); δ† (80 MHz) 9.80 (1 H, s, CHO), 4.56 (1 H, br s, O–CH–O), 4.40—4.10 [2 H, complex, 1-H (δ 4.19, br d, J 6 Hz) and 5-H], 4.05—3.20 (4 H, complex m, 2 × OCH_2), and 2.5—0.9 [26 H, complex, 2-H_{endo}, 3-H (δ 2.03, m), 4-, 6-, and 7-H_2, and 9 × CH_2], the trans-*aldehyde* (**18**) [79 mg, 40% from (**16**)]; t.l.c. one component, R_F 0.34 [acetone–light petroleum (1:5)]; $v_{max.}$ 1 725 cm^{-1} (C=O); δ * (80 MHz) 9.65 (1 H, s, CHO), 4.56 (1 H, br s, O–CH–O), 4.46 (2 H, br m, 1- and 5-H), 4.05—3.20 (4 H, complex m, 2 × OCH_2), 2.72 (1 H, complex m, 3-H), and 2.3—1.0 (25 H, complex, 2-H, 4-, 6-, and 7-H_2, and 9 × CH_2), and a mixture of the cis- and trans-aldehydes (**17**) and (**18**) [30 mg, 15% from (**16**)].

trans-3-[(E)-3-*Oxo-oct-1-enyl*]-exo-2-[7-(*tetrahydropyran-2-*

heptyl]-8-*oxabicyclo*[3.2.1]*octane* (**19**).—Sodium hydride (7.0 mg, 0.29 mmol) was added to a solution of dimethyl (2-oxoheptyl)phosphonate (67 mg, 0.30 mmol) in dry THF (3 ml), and the mixture was vigorously stirred at room temperature under argon for 2.5 h. A solution of the trans-aldehyde (**18**) (71 mg, 0.21 mmol) in dry THF (1 ml) was then rapidly added to the white viscous mixture and the mixture was stirred for a further 3 h. The mixture was then neutralised with acetic acid (0.1M in ether) and concentrated, and the residue was partitioned between aqueous sodium chloride (2%) and ether. The combined extracts were washed successively with saturated aqueous sodium hydrogen carbonate, water, and saturated aqueous sodium chloride, dried, and concentrated. The residual oil was purified by l.p.l.c. (Kieselgel 60 H, 20 g) [acetone–light petroleum (1:12) as eluant] to give the trans-*enone THP ether* (**19**) (53 mg, 58%) as an oil (Found: M^+, 434.3408. $C_{27}H_{46}O_4$ requires M, 434.3396); t.l.c. one component, R_F 0.36 [acetone–light petroleum (1:5)]; $\lambda_{max.}$ 230 nm (ε 10 000 dm^3 mol^{-1} cm^{-1}); $v_{max.}$ 1 690, 1 670 (conj. C=O), 1 625 (conj. CH=CH), and 980 cm^{-1} (*trans* CH=CH); δ * (80 MHz) 6.77 (1 H, dd, J 16 and 6 Hz, C*H*=CHCO), 5.98 (1 H, dd, J 16 and 1.5 Hz, CH=C*H*CO), 4.56 (1 H, br s, O–CH–O), 4.38 (2 H, br s, 1- and 5-H), 4.03—3.21 (4 H, complex m, 2 × OCH_2) 2.9—2.35 [3 H, complex, 3-H and CH=CHCOC*H*_2$ (δ 2.52, t, J 7 Hz)], 2.15—1.0 (31 H, complex, 2-H, 4-, 6-, and 7-H_2, and 12 × CH_2), and 0.89 (3 H, t, J 6 Hz, Me).

exo-2-(7-*Hydroxyheptyl*)-trans-3-[(E)-3-*oxo-oct-1-enyl*]-8-*oxabicyclo*[3.2.1]*octane* (**20**).—Aqueous hydrochloric acid (7%; 0.16 ml, 0.3 mmol) was added to a solution of the enone (**19**) (30 mg, 0.069 mmol) in 95% ethanol (2.5 ml) and the mixture was stirred at 75 °C for 0.5 h. The cooled mixture was neutralised with aqueous sodium hydrogen carbonate, diluted with water (20 ml), saturated with sodium chloride, and then extracted with ether (4 × 6 ml). The combined extracts were washed with aqueous sodium chloride (20%, then saturated), dried, concentrated, and dried *in vacuo* (0.1 mmHg) to afford the *enone alcohol* (**20**) (24 mg, 99%) as a pale yellow oil (Found: M^+, 350.2825. $C_{22}H_{38}O_3$ requires M, 350.2821); t.l.c. one component, R_F 0.46 [acetone–light petroleum (1:1)]; $\lambda_{max.}$ 229 nm (ε 8 500 dm^3 mol^{-1} cm^{-1}); $v_{max.}$ 3 300 (O–H), 1 690, 1 670 (conj. C=O), 1 625 (conj. CH=CH), and 985 cm^{-1} (*trans* CH=CH); δ * (80 MHz) 6.77 (1 H, dd, J 16 and 6 Hz, C*H*=CHCO), 5.98 (1 H, dd, J 16 and 1.5 Hz, CH=C*H*CO), 4.38 (2 H, br s, 1- and 5-H), 3.64 (2 H, t, J 6 Hz, C*H*_2OH), 2.9—1.0 [29 H, complex, 2- and 3-H, 4-, 6-, and 7-H, CH=CHCOC*H*_2 (δ 2.52, t, J 7 Hz), 9 × CH_2, and OH], and 0.89 (3 H, t, J 6 Hz, Me).

7-{endo-3-[(E)-3-*Oxo-oct-1-enyl*]-8-*oxabicyclo*[3.2.1]*oct-trans-2-yl*}*heptanoic Acid* (**21**).—Pyridinium dichromate (90 mg, 0.24 mmol) was added in one portion to a stirred solution of the enone alcohol (**20**) (20 mg, 0.067 mmol) in dry DMF (0.75 ml) and the resultant solution was stirred in a dry atmosphere for 14 h and then added to aqueous sodium carbonate (1M; 10 ml). The mixture was washed with ether and then acidified to pH 1 with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ether (4 × 3 ml). The combined extracts were washed with saturated aqueous sodium chloride, dried, concentrated, and dried at 50 °C *in vacuo* (0.2 mmHg) to afford the *enone acid* (**21**) (17 mg, 82%) as an oil (Found: M^+, 364.2620. $C_{22}H_{36}O_4$ requires M, 364.2614); t.l.c. one component, R_F 0.34 [ethyl acetate–cyclohexane–formic acid (40:40:1)]; $\lambda_{max.}$ 229 nm (ε 7 500 dm^3 mol^{-1} cm^{-1}); $v_{max.}$ 3 600—2 500 (3 160) [C(O)O–H], 1 710 (C=O, carboxylic acid), 1 670 (conj. C=O), 1 625 (conj. CH=CH), and 985 cm^{-1} (*trans* CH=CH); δ * (80 MHz) 8.2—7.3 (1 H, br s, CO_2H), 6.77 (1 H, dd, J 16 and 6 Hz, C*H*=CHCO), 5.98 (1 H, dd, J 16 and 1.5 Hz, CH=C*H*CO), 4.38 (2 H, br s, 1- and 5-H), 2.9—1.0 [28 H, complex, 2-and 3-H,

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* Unprimed locants refer to oxabicyclo-octa(e)ne ring.

4-, 6-, and 7-H_2, CH=CHCOCH_2 (δ 2.52, t, J 7 Hz), CH_2CO$_2$H (δ 2.32, t, J 7 Hz), and 8 × CH$_2$], and 0.89 (3 H, t, J 6 Hz, Me).

7{endo-3-[(E)-3-*Hydroxyoct*-1-*enyl*]-8-*oxabicyclo*[3.2.1] *octan*-trans-2-*yl*}*heptanoic Acid* (1).—A solution of L-Selectride (1.0$_M$; 0.12 ml, 0.12 mmol) in THF was added dropwise to a stirred solution of the enone acid (21) (15 mg, 0.041 mmol) in dry THF (1.2 ml) maintained at −78 °C under argon. The resultant solution was stirred at −78 °C for 0.4 h, at between −78 and 0 °C for 4 h, and at 0 °C for 0.8 h. The solution was then treated dropwise successively with aqueous sodium hydroxide (3$_M$; 0.3 ml) and aqueous hydrogen peroxide (30%; 0.2 ml), stirred at 0 °C for 0.5 h, diluted with water (10 ml), and washed with ether. The aqueous solution was then acidified to pH 2 with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ether (4 × 4 ml). The combined extracts were washed with aqueous sodium chloride (20%, then saturated), dried, concentrated, and dried *in vacuo* (0.1 mmHg) to give the TXA$_1$ analogue (1) (14 mg, 93%) as a mixture of diastereoisomeric alcohols (1a and b) (Found: M^+, 366. C$_{22}$H$_{38}$O$_4$ requires M, 366); t.l.c. two components, R_F 0.29 and 0.25 [ethyl acetate–cyclohexane–formic acid (40:40:1)]; $v_{max.}$ 3 600—2 400 (3 370) (CO$_2$H, OH), 1 710 (C=O), and 975 cm^{-1} (*trans* CH=CH); δ* (80 MHz) 5.75—4.9 (4 H, complex, CH=CHCHOH (δ 5.60, dd, J 16 and 6 Hz), CH=CHCHOH (δ 5.33, dd, J 16 and 6 Hz), CO$_2$H, and CHOH], 4.35 (2 H, br s, 1- and 5-H), 4.08 (1 H, br q, J 6 Hz, CHOH), 2.75—1.05 [28 H, complex, 2- and 3-H, 4-, 6-, and 7-H$_2$, CH_2CO$_2$H (δ 2.32, t, J 7 Hz), and 9 × CH$_2$], and 0.89 (3 H, t, J 6 Hz, Me).

The sample for biological evaluation was purified by l.p.l.c. (Kieselgel 60 H, ethyl acetate as eluant) (82% recovery).

9-*Oxabicyclo*[4.2.1]*nonane*-2,3-*diol* (27) *and* 9-*Oxabicyclo*-[4.2.1]*nonane*-3,4-*diol* (28).—A stirred solution of 9-oxabi-cyclo[4.2.1]non-2-ene[10] (25) and 9-oxabicyclo[4.2.1]non-3-ene[10] (26) (5:1) (5.0 g, 0.04 mol) in formic acid (98—100%; 13.3 g, 0.29 mol) was heated at 45 °C and aqueous hydrogen peroxide (30%; 5.2 g, 0.046 mol) was added during 1.5 h, the internal temperature being kept at 45—60 °C. Most of the formic acid was then removed under reduced pressure and the residual crude monoformyl esters were hydrolysed by steam distillation until 10 ml of aqueous formic acid distillate had been collected. The residue was concentrated and dried *in vacuo* (0.05 mmHg) to yield the diols (27) and (28) (5.3 g, 83%) as a light brown syrup (Found: M^+, 158.0940. C$_8$H$_{14}$O$_3$ requires M, 158.0943); t.l.c. one component, R_F 0.45 [ether–methanol (4:1)]; $v_{max.}$ 3 390 cm^{-1} (O–H); δ (80 MHz) 4.6—4.2 (2 H, br complex m, CHOCH), 4.1—3.2 (4 H, br complex m, 2 × CHOH), and 2.6—1.3 (8 H, br complex m, ring CH$_2$).

3-*Formyl*-8-*oxabicyclo*[3.2.1]*oct*-2-*ene* (31) *and* 2-*Formyl*-8-*oxabicyclo*[3.2.1]*oct*-2-*ene* (32).—A solution of the diols (27) and (28) (1.6 g, 10 mmol) in water (2 ml) was added in one portion to a stirred solution of sodium metaperiodate (2.6 g, 12 mmol) in water (32 ml) at 20 °C, and the mixture was stirred

until the exothermic reaction had subsided and the temperature had dropped from 29 to 25 °C. The reaction mixture was immediately added to a mixture of aqueous potassium hydr-oxide (5%; 40 ml) and ether (100 ml), and then vigorously stirred under nitrogen for 0.5 h at 20 °C. The ethereal layer was then separated, the aqueous layer extracted with ether (2 × 50 ml), and the combined ethereal layers washed with saturated aqueous sodium chloride, dried, and concentrated. The residual oil was distilled (short-path) to give a mixture (1:1) of the cyclised aldehydes (31) and (32) as an oil, b.p. 45—55 °C at 0.05—0.1 mmHg (Found: M^+, 138.0684. C$_8$H$_{10}$O$_2$ requires M, 138.0681); t.l.c. one component, R_F 0.33 (ether); $\lambda_{max.}$ 228 nm (ϵ 7 000 dm^{-3} mol^{-1} cm^{-1}); $v_{max.}$ 1 675 (C=O) and 1 635 cm^{-1} (C=C); δ (100 MHz) 9.42 and 9.35 (together 2 H, 2 × s, 2 × CHO), 6.94 (1 H, dt, J 4.4 and 1.7 Hz, OCHCH=CCHO), 6.59 (1 H, ddd, J 4.4, 2.9, and 1.5 Hz, CH$_2$CH=CCHO), 4.95 [1 H, d, J 5 Hz, OCHC(CHO)=CH], 4.67 (3 H, complex m, 3 × OCH), 2.91 and 2.73 (together 2 H, d of br m, J 18 Hz and dd,J17and5Hz,2 × *exo*-CHC=C),and2.4—1.4(10H,complex, 2 × *endo*-CHHC=C and 2 × CHCH_2CH_2CH).

Acknowledgements

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* Unprimed locants refer to oxabicyclo-octa(e)ne ring.