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SYNTHESIS OF RACEMIC AND OPTICALLY ACTIVE FORMS OF LINEATIN, THE UNIQUE TRICYCLIC PHEROMONE OF *TRYPODENDRON LINEATUM* (OLIVIER)†

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Abstract—(±) - 3,3,7 - Trimethyl - 2,9 - dioxatricyclo[3.3.1.$0^{4,7}$]nonane **1** and (±) - 3,3,7 - trimethyl - 2,9 - dioxatricyclo[4.2.1.$0^{4,7}$]nonane **2** were synthesized. The former was shown to be (±)-lineatin, an ambrosia beetle pheromone. A selective synthesis of (±)-lineatin was devised, which was modified to yield the both enantiomers of lineatin *via* optical resolution of an intermediate.

Lineatin is an attractant compound isolated from frass produced by female beetles of *Trypodendron lineatum* (Olivier) boring in Douglas fir.[1] Its structure has been proposed by Silverstein *et al.* to be one of the two isomeric tricyclic acetals **1** or **2** without assignment of the absolute configuration.[1] A synthesis of a mixture of **1** and **2** was also reported which could afford neither pure **1** nor **2**.[1] The proposed structures suggest a possible biogenetical relationship between lineatin and grandisol **3**, one of the components of the boll-weevil pheromone.[2] In continuation of our work on the synthesis of the optically active forms of grandisol,[3,4] we undertook the synthetic studies on lineatin. This paper described (i) a synthesis of the racemetes of **1** and **2** establishing the structure of lineatin as **1**[5] (ii) a selective synthesis of (±)-**1**, and (iii) a synthesis of (1*S*, 4*R*, 5*S*, 7*S*) - (+) - **1** and its antipode which enables the elucidation of stereochemistry-pheromone activity relationship.

Synthesis of (±) - 3,3,7 - *trimethyl* - 2,9 - *dioxatricyclo*[3.3.1.$0^{4,7}$]*nonane* **1** *and* (±) - 3,3,7 - *trimethyl* - 2,9 - *dioxatricyclo*[4.2.1.$0^{4,7}$]*nonane* **2**

A retrosynthetic analysis of the target molecule **1** or **2** was made as shown in Fig. 1. The tricyclic compound **1** and **2** is an intramolecular acetal derivable from a dihydroxy aldehyde **A** or **B**, respectively. These tetrasubstituted cyclobutanes **A** or **B** is in turn derivable from bicyclo[3.2.0]heptane compounds **C** or **D**, respectively. A mixture of **C** and **D** is obtainable by the photo-cycloaddition of vinyl acetate **4** to 3 - methylcyclopent - 2 - en - 1 - one **5**. In the course of synthesis, **C** and **D** or their equivalents must be separated and their structures should be rigorously determined so as to lead unambiguously to each of the compounds **1** and **2**.

†Pheromone Synthesis-XXXVII. This work was presented at the EUCHEM Conference on Chemistry of Insects at Borgholm, Öland, Sweden, on August 14, 1979, as a part of K. M.'s lecture. The experimental part of this work was taken from the Ph.D. dissertation of M. S. (September, 1979). Part XXXVI, K. Mori and H. Iwasawa, *Tetrahedron* **36**, 2209 (1980).

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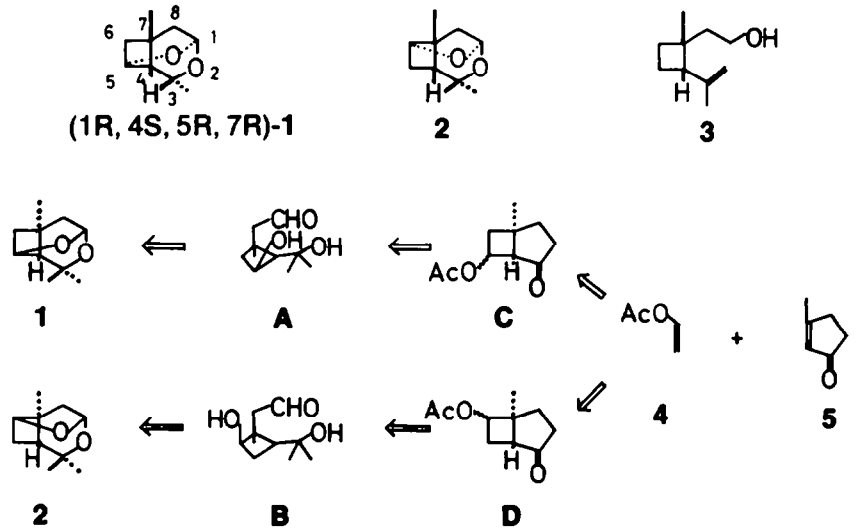


Fig. 1.

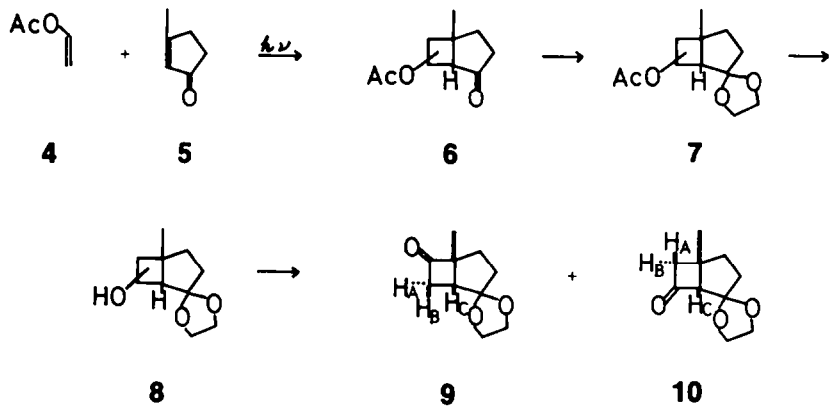


Fig. 2.

The first step of our synthesis was thus irradiation of vinyl acetate **4** and the enone **5**[6] to give the adduct **6** in 60% yield as a mixture of four possible regio- and stereoisomers. Since it was impossible to completely separate the four isomers by chromatographic means, the mixture **6** was employed directly for the next step. Treatment of **6** with butanone ethyleneketal in the presence of p-TsOH gave a mixture **7** of acetoxy ketals. This was converted to a mixture **8** of hydroxy ketals by mild transesterification with KCN in 95% EtOH.[7] Oxidation of **8** with pyridinium chlorochromate (PCC)[8] gave a mixture of two isomeric ketones **9** and **10**. By this transformation the number of the isomers was reduced from four to two. These two ketones were cleanly separable by chromatography over silicic acid. The major product (78% of the total) was eluted in earlier fractions and the structure **9** was assigned to it on the basis of its NMR data indicating the presence of a proton (H_C) vicinal to the two methylene protons (H_A and H_B): δ (100 MHz, CCl_4) 2.24 (1H, dd, $J_{AC} = 6$, $J_{BC} = 10$ Hz, H_C), 2.80 (1 H, dd, $J_{AC} = 6$, $J_{AB} = 20$ Hz, H_A), 3.16 (1 H, dd, $J_{BC} = 10$, $J_{AB} = 20$ Hz, H_B). The minor product **10** (22% of the total) was eluted later and the structure **10** was supported by its NMR spectrum in which a singlet due to the angular proton (H_C) was observed: δ 2.62 (1 H, dd, $J_{(long\ range)} = 4$, $J_{AB} = 20$ Hz, H_A), 2.80 (1 H, s, H_C), 2.90 (1 H, dd, $J_{(long\ range)} = 2$, $J_{AB} = 20$ Hz, H_B).

The next problem was the stereoselective reduction of the ketones **9** and **10** to *endo*-alcohols *endo*-**8a** and *endo*-**8b** (Fig. 3). The high stereoselectivity in this step is essential in executing the synthesis, because the *exo*-isomers can give neither **1** nor **2** at the final stage of intramolecular acetalization. Four kinds of metal hydrides were tested for this purpose employing the major ketone **9** as the substrate (Table 1). The most selective reagent was L-selectride[Li(sec-Bu)$_3$BH][9] in THF, which yielded a mixture of an *endo*-**8a** (89%) contaminated with a small amount (11%) of its *exo*-isomer. The *endo*-stereochemistry of the major alcohol *endo*-**8a** was assigned on the basis of the NMR evidence that a 3 H-singlet due to the angular Me group shifted less significantly upon addition of Eu(fod)$_3$† in the case of the major isomer (δ 1.15→1.27) than in the case of the minor one with *exo*-stereochemistry (δ 1.10→1.52). The complete separation of these two stereoisomers was

†Tris(6,6,7,7,8,8,8 - heptafluoro - 2,2 - dimethyl - 3,5 - octanedionato)europium (III).

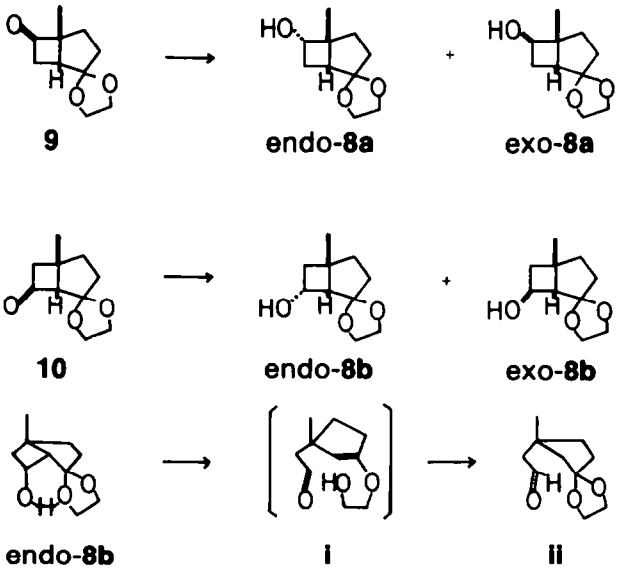


Fig. 3.

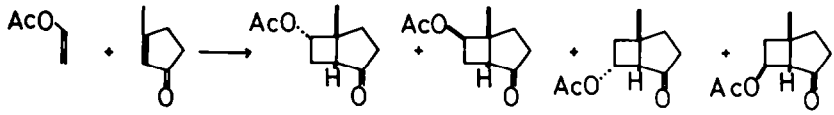
Table 1. Reduction of the ketone **9** with metal hydrides

Reducing agent	Product ratio (%)	
	endo-8a	exo-8a
$NaBH_4$	75	25
$Li(sec\text{-}Bu)_3BH$	89	11
$LiAlH_4$	64	36
$LiAl(OBu^t)_3H$	52	48

rather difficult and the synthesis was carried through to completion employing 89% pure *endo*-**8a**. It should be mentioned that *exo*-**8a** could not yield any intramolecular acetal because of the unfavorable orientation of the OH group and hence caused no trouble in securing the final product. The ketone **10** was also reduced with L-selectride to give essentially a single product showing a 3 H-singlet at δ 1.18 (in CCl_4) in its NMR spectrum. After 20 hr at room temperature the sample in CCl_4 decomposed to a compound with a signal at δ 9.60 (1 H, -CHO). This was explained as follows: the reduction product was *endo*-**8b** and it decomposed to an aldehyde **ii** by a retroaldol reaction catalyzed by a trace of acid in CCl_4 via an intermediate **i**. This piece of chemical evidence for *endo*-stereochemistry of the reduction product was supported later by its conversion to (±)-**1**.

Comparison of the NMR spectra of *endo*-**6a** and *endo*-**6b** with that of the mixture **6** enabled us to deduce the product ratio of the initial photo-cycloaddition reaction. The photo-adduct mixture **6** showed three singlet signals (δ 1.15, 1.30, 1.35) due to the angular Me and two singlet signals (δ 1.80, 1.97) due to OAc. Upon addition of $Eu(fod)_3$, the signals were separated and all of the eight signals due to Me and OAc became discernible when a sufficient amount of $Eu(fod)_3$ was added[$Eu(fod)_3$: **6** = 4:3(w/w)]. By measuring the NMR spectra of *endo*-**6a** and *endo*-**6b** under the same condition as for **6**, assignment of each two signals to each of the four isomers (*endo*-**6a**, *exo*-**6a**, *endo*-**6b** and *exo*-**6b**) became possible (Table 2). The photo-adduct was composed of 45:31:13:11 of *exo*-**6a**, *endo*-**6a**, *exo*-**6b** and *endo*-**6b**. Therefore the ratio of **6a** (head-to-tail adduct) to **6b** (head-to-head adduct) was 3:1. It was also found that a signal due to CHOAc of **6a** appeared as a seemingly triplet (δ 4.82, J = 6 Hz), while that of **6b** was observed as an AB-type quartet (δ 5.08, J = 6 Hz). This finding was

Table 2. Ratio of the regio- and stereoisomers produced by the photo-cycloaddition reaction (4 + 5 → 6)



4 **5** **endo-6a** **exo-6a** **endo-6b** **exo-6b**

Isomers	NMR (δ-value)[a] of		Composition of the synthetic products					
	5-Me	OAc-Me	6[b]		endo-6a[c]		endo-6b[d]	
endo-6a	2.08	3.10	30.8%[e]	(31.7%)[f]	97.9%[e]	(97.8%)[f]	0%[e]	(0%)[f]
exo-6a	1.84	2.96	44.1	(44.6)	2.1	(2.2)	0	(0)
endo-6b	1.60	4.04	11.2	(10.5)	0	(0)	99.5	(99.5)
endo-6b	2.24	4.88	13.9	(13.2)	0	(0)	0.5	(0.5)

[a] Measured in the presence of 1.33 (w/w) fold of $Eu(fod)_3$.

[b] A mixture obtained by photo-cycloaddition of 4 to 5.

[c] A mixture obtained by reduction of 9 with L-selectride (after chromatographic purification).

[d] A mixture obtained by reduction of 10 with L-selectride (without chromatographic purification).

[e] Calculated from the signal areas of 5-Me.

[f] Calculated from the signal areas of OAc-Me.

very useful later in deducing the structure of the photo-adduct **26**. Vandewalle *et al.* also found the predominance of the head-to-tail adduct in the photocycloaddition of electron-rich olefins to cyclopentenones. Their as well as our own results indicate that the electronic effect is more important than the steric effect in determining the regio-selectivity of this particular photocycloaddition reaction.

In order to cleave the five-membered ring, the *endo*-alcohols **8a** and **8b** were converted to trimethylsilyl enol ethers **12** and **14**, whose olefinic linkage was oxidized with ozone (Fig. 4). Acetylation of *endo*-**8a** gave the corresponding acetate **11**, which was heated in 50% AcOH aq to give *endo*-**6a**. This acetoxy ketone was treated with lithium diisopropylamide (LDA) and Me_3SiCl in THF to give **12**. The structure **12** was supported by the IR (ν_{max} 3050 cm^{-1}; –C=CH–) and NMR (δ 4.55; 1 H; –C=CH–) spectra. In the same manner, *endo*-**8b** was converted to the silyl enol ether **14** (ν_{max} 3050 cm^{-1}; δ 4.70, 1 H) *via* **13** and *endo*-**6b**.

Ozonization of the enol ether **12** was carried out in CH_2Cl_2 with O_3. Reductive work-up (Ph_3P) of the ozonide followed by mild acid-treatment (AcOH) and esterification with CH_2N_2 gave an aldo ester **15**. This was treated with methyl ethylene orthoformate and *p*-TsOH in CH_2Cl_2 to yield an acetal ester **16**. This was added to an excess of MeMgI in ether and the reaction mixture was acidified with dil. HCl to give (±) - 3,3,7 - trimethyl - 2,9 - dioxatricyclo[4.2.1.$0^{4,7}$]nonane **2**. Its IR, NMR and mass spectral data were quite different from those of lineatin.[1] The proposed structure **2** was therefore excluded. The synthesis of a racemate with the alternative structure **1** was carried out in the same manner via **17** and **18** starting from the isomeric silyl enol ether **14**. The spectral properties of (±)-**1** were in good accord with the published data of lineatin. The complicated fingerprint region of the IR spectrum of our (±)-**1** coincided with that of lineatin.

The structure of lineatin was thus established as 3,3,7 - trimethyl - 2,9 - dioxatricyclo[3.3.1.$0^{4,7}$]nonane **1**. The racemic lineatin was biologically active when tested on *Trypodendron lineatum*.[11,12]

Selective synthesis of (±)-*lineatin*

In order to develop a synthetic route to the optically active forms of lineatin **1**, we felt it necessary to devise a more selective synthetic route to (±)-**1**. Our synthesis as described above produced more of the undesired isomer **2** than (±)-**1**, for the initial photo-cycloaddition yielded the desired adduct **6b** only as a minor product (24% of the total). The best way to circumvent this difficulty was to use other cyclopentenones as the starting material in which the effect of the electron-withdrawing CO group is operating in the opposite direction as compared to that in **5**. This and other considerations led us to the retrosynthetic scheme shown in Fig. 6. (±)-Lineatin **1** is obtainable from a keto lactone **E** by reduction and cyclization. This lactone **E** can be synthesized from a hydroxy ketone **F**, which is derivable from a ketone **G** by a 1,2-CO transposition. The initial step of the synthesis is the photo-cycloaddition of vinyl acetate **4** to a cyclopentenone **19**.

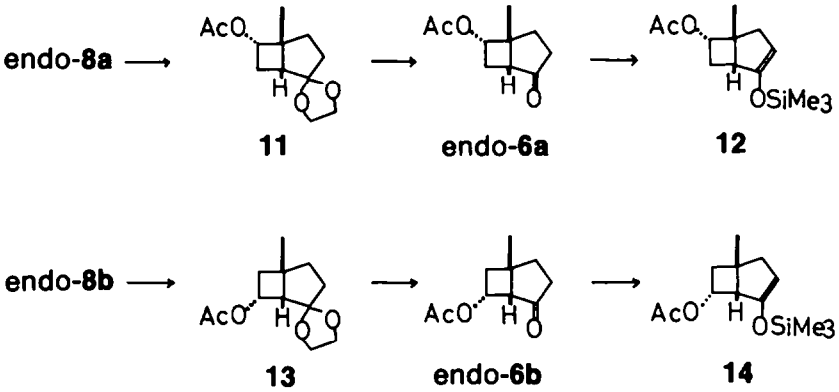


Fig. 4.

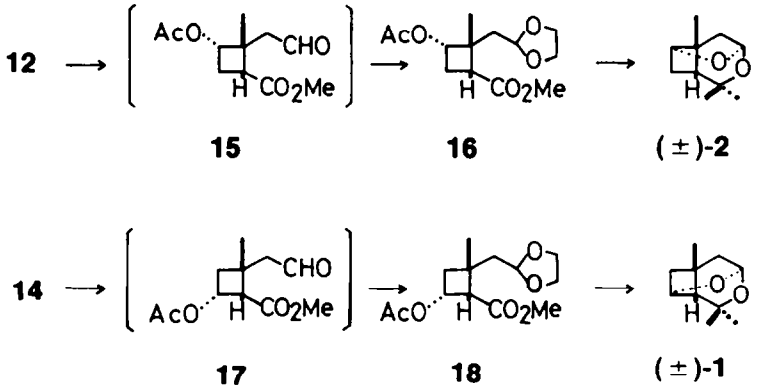


Fig. 5.

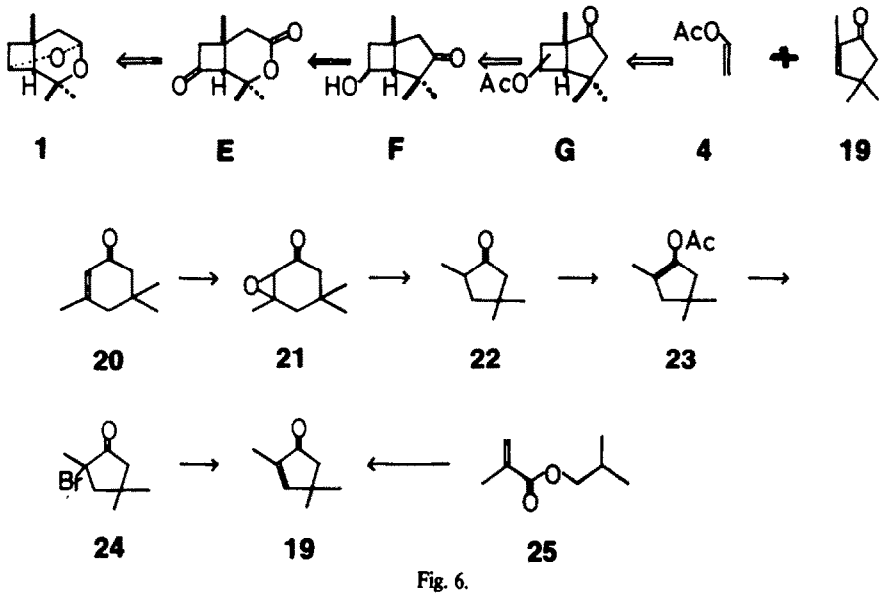


Fig. 6.

Our first task was therefore the preparation of 2,4,4 - trimethylcyclopent - 2 - en - 1 - one **19**. Although this was a known compound,[13,14] we felt it necessary to develop another synthesis suitable for a large-scale preparation. According to the procedure of House *et al.*[15,16] isophorone **20** was converted to 2,4,4 - trimethylcyclopentan - 1 - one **22** via isophorone oxide **21**. Treatment of **22** with Ac_2O–$HClO_4$ gave an enol acetate **23**. This was brominated with N-bromosuccinimide to give **24**. Dehydrobromination of **24** with Li_2CO_3 in C_5H_5N yielded the desired cyclopentenone **19** in 40% over-all yield from isophorone **20**. After the completion of this work, however, Gowda and McMurry published a one-step synthesis of **19**[17] using Conia's method of cyclopentenone construction.[18] They prepared **19** by simply heating isobutyl methacrylate **25** in polyphosphoric acid (PPA) at 100° for 13.5 hr.[17] We adopted their method and were able to prepare **19** in 50% yield by heating **25** in PPA at 100° for 5–10 min.

Photo-cycloaddition of vinyl acetate to the enone **19** was a little bit more complicated than that to **5** (Figs. 7 and 8). After 60 hr irradiation 50% of the starting enone **19** was consumed, and five products were observed by GLC. In its NMR spectrum the product mixture exhibited signals due to CHOAc at $\delta \sim 4.00$, ~ 4.60, ~ 4.80 and ~ 5.20, a signal due to CHO at $\delta \sim 9.50$. This suggested the occurrence of a side-reaction which destroyed the acetoxy ketones **26** by a Norrish Type I-like process (Fig. 8, **26**→**27**). The reaction was therefore stopped after 60 hr and a resulting mixture of the starting materials and the products was carefully distilled to give a mixture of **26a** and **26b**. An inspection of the NMR spectrum of the mixture allowed us to estimate the ratio of **26a** to **26b** as 2:3 by integrating the signal areas due to CHOAc, which appeared as triplet in the case of **26a** and as quartet in the case of **26b**. Since the separation of the two ketones **26a** and **26b** was difficult, the mixture was used as such for the next step, assuming that the separation might be possible at a later stage.

The next task was the transposition of the CO group

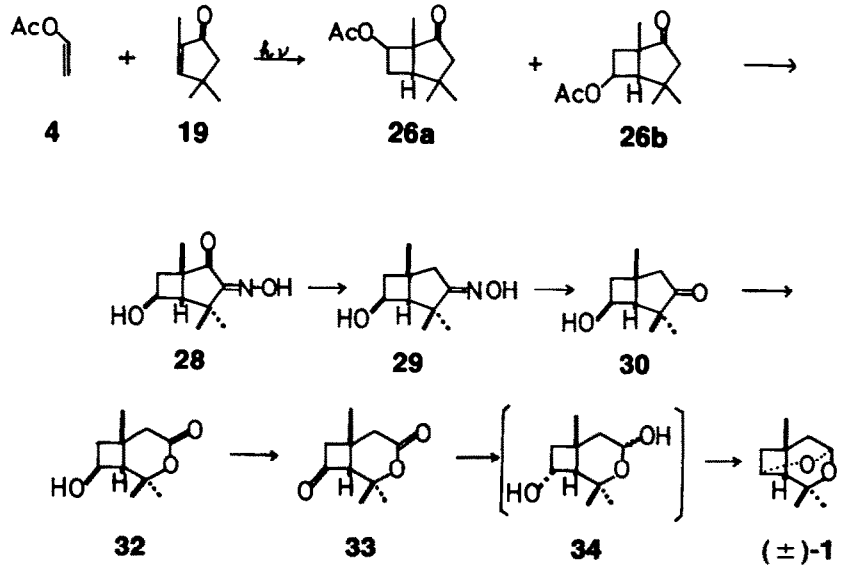


Fig. 7.

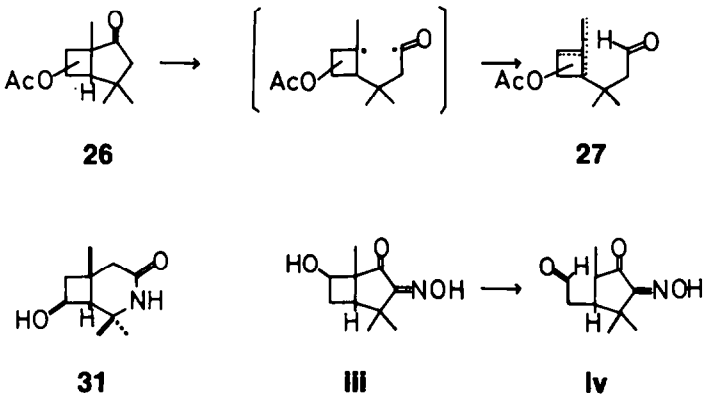


Fig. 8.

from C-2 to C-3. After several unsuccessful attempts to execute this 1,2-CO transposition by Trost's sulfenylation procedure,[19] we adopted the route shown in Fig. 7. This nitrosation-reduction procedure was used recently by Ayer and Browne in their synthesis of (±)-grandisol 3.[20] The acetoxy ketone mixture (**26a** + **26b**) in C_6H_6 was treated with *i*-AmONO in the presence of *t*-AmOK. Chromatographic purification of the product afforded in 30% yield a mixture of *syn*- and *anti*-oximes **28**. Isoamyl acetate was also obtained as a by-product generated by transesterification. No other product was isolated except resinous material which presumably resulted from the retroaldol reaction (Fig. 8, iii→iv) of the isomeric and undesired keto-oxime iii followed by resinification of the aldehyde iv. This side-reaction unexpectedly solved the problem of the separation of regio-isomers, and we were able to obtain only the desired product **28** as a crystalline solid. The Wolff–Kishner reduction of **28** with KOH (1.5 eq) and N_2H_4 in ethylene glycol at 150° gave a crystalline oxime **29** in 52% yield. The conventional severe reaction condition (use of a large excess of KOH and reaction temperature as high as 200°) was deteriorative in the present case. The oxime **29** was smoothly converted to the desired ketone **30** in 55% yield by treatment with $TiCl_3$. A crystalline lactam **31** was obtained as a by-product resulting from the Beckmann rearrangement of **29**.

The hydroxy ketone **30** was treated with *m*-chloroperbenzoic acid in the presence of $NaHCO_3$ to effect Baeyer–Villiger oxidation giving a hydroxy lactone **32** in 95% yield. Reduction of this lactone **32** with diisobutylaluminum hydride (DIBAH) did not yield (±)-lineatin **1**. This meant that the OH group in **28**, **29**, **30**, **31** and **32** was in *exo*-configuration as depicted in the formulas. The configuration of the OH group was therefore inverted by first oxidizing the hydroxy lactone **32** to a keto lactone **33** and subsequently reducing **33** with DIBAH to the desired *endo*-hydroxy lactol **34**. Acidification of the reaction mixture effected the final intramolecular acetalization and (±)-lineatin **1** was obtained by merely distilling the crude product with no need of chromatographic purification. The physical data (glc, IR, NMR and MS) of this product was identical with those of the previously synthesized one.

Synthesis of optically active forms of lineatin

After the completion of the selective synthesis of (±)-lineatin, we turned our attention to the synthesis of lineatin enantiomers. An initial attempt to resolve the keto lactone **33** was fruitless. We therefore chose the hydroxy ketone (±)-**30** as a candidate for optical resolution. The racemic ketol **30** was treated with an optically active isocyanate (*S*)-(+)-**35** to give a diastereomeric mixture of the carbamates **36** and **37** *cf.*[21] These were separated by chromatography over a Merck Lobar column to give **36**, m.p. 47–48°, and **37**, m.p. 110–111°. HPLC analysis of the separated isomers showed that our **36** was contaminated with 7.75% of **37** and our **37** contained 6.00% of **36**. The carbamates **36** and **37** were treated with 3% EtONa in EtOH to give crystalline (−)-**30** and (+)-**30**, respectively. From the HPLC analytical data of **36** and **37**, the optical purities of (−)-**30** and (+)-**30** were estimated to be 84.5 and 88.0%, respectively. The (−)-ketol **30** showed a negative Cotton effect ($[\theta]_{292} - 1560°$), while (+)-**30** exhibited a positive Cotton effect ($[\theta]_{292} + 1610°$) in their CD. The octant projection

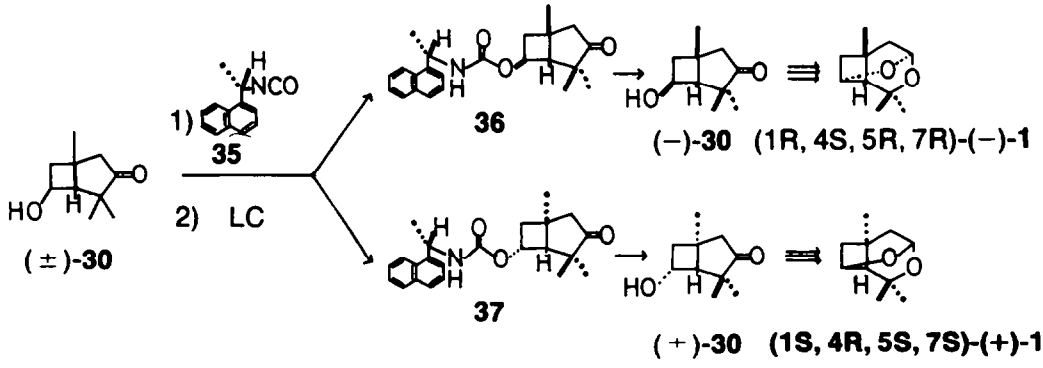


Fig. 9.

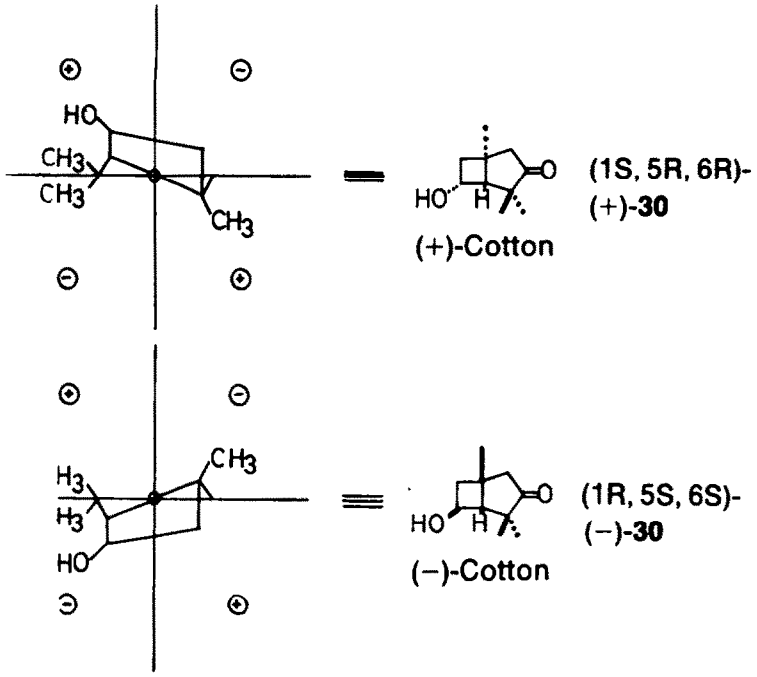


Fig. 10.

(Fig. 10) of the ketols **30** allowed the assignment of absolute stereochemistry of (−)-**30** as 1*R*, 5*S*, 6*S* and that of (+)-**30** as 1*S*, 5*R*, 6*R* on the basis of the octant rule.

These ketols (−)-**30** and (+)-**30** were converted to (1*R*, 4*S*, 5*R*, 7*R*)-(−)-lineatin **1**, $[\alpha]_D^{22} - 40°$ (*n*-pentane) and (1*S*, 4*R*, 5*S*, 7*S*)-(+)-lineatin **1**, $[\alpha]_D^{22} + 36°$ (*n*-pentane) in the same manner as described for the racemate. Since the available amount of our synthetic lineatin enantiomers was very limited, we were unable to measure accurate $[\alpha]_D$ values. Their ORD curves were measured in a qualitative manner and (−)-**1** exhibited a negative plain curve while (+)-**1** showed a positive plain curve. Some intramolecular ketal pheromones with positive plain ORD curves are known such as (1*R*, 5*S*) - (+) - frontalin **38**[22] and (1*R*, 5*S*, 7*R*) - (+) - *exo* - brevicomin **39**[22] and (1*R*, 2*S*, 4*R*, 5*S*) - (+) - *α* - multistriatin **40**.[23]

Figure 11 shows projections of (+)-**1**, (+)-**38**, (+)-**39** and (+)-**40** in which two ether O atoms are laid in the front side. The similarities among them are self-evident. Recently Snatzke *et al.* studied the chiroptical properties of 2,9-dioxatricyclo[4.3.1.0^{3,7}]decane system and found that those represented by projectional formula **41** show positive plain curves in their ORD.[24] The projection of (+)-lineatin **1** as shown in Fig. 11 is quite similar to **41**. These considerations support the (1*S*, 4*R*, 5*S*, 7*S*)-absolute stereochemistry of (+)-lineatin which is consistent with the previous assignment based on the CD analysis of the ketone (+)-**30**.

In conclusion, we established the structure of lineatin as 3,3,7 - trimethyl - 2,9 - dioxatricyclo[3.3.1.0^{4,7}]nonane **1** by an unambiguous synthesis and prepared its (1*S*, 4*R*, 5*S*, 7*S*) - (+) - and (1*R*, 4*S*. 5*R*, 7*R*) - (−) - enantiomers.

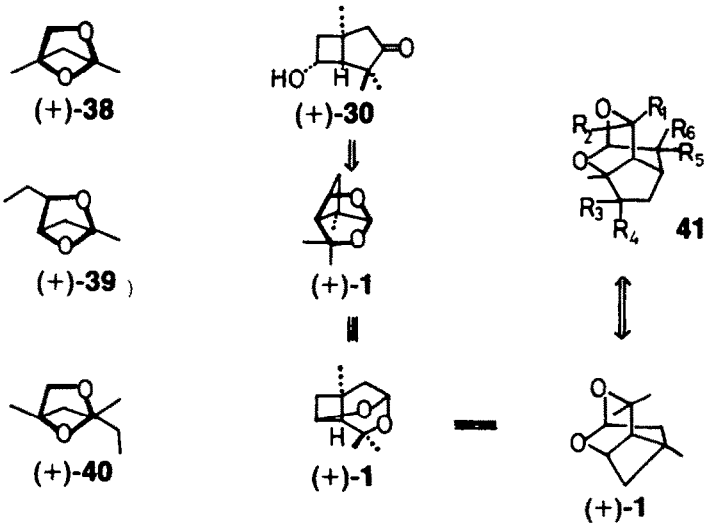


Fig. 11.

The biological activities of the optically active forms of lineatin are under investigation by Prof. J. P. Vité, University of Freiburg.

EXPERIMENTAL

All b.ps and m.ps were uncorrected. IR spectra refer to films and were recorded on a JASCO IRA-1 spectrometer unless otherwise stated. NMR spectra were recorded with TMS as an internal standard on a Hitachi R-24A spectrometer (60 MHz) or on a JOEL JNM-MH 100 spectrometer (100 MHz). Optical rotations were measured on a JASCO DIP-181 digital polarimeter. CD spectra were recorded on a JASCO J-500A polarimeter equipped with a computerized data processor. ORD spectra were measured on a JASCO ORD/UV-5 polarimeter. Glc analyses were performed on a Yanagimoto 550F gas chromatograph. HPLC analyses were carried out on a Shimadzu LC-2 or on a Shimadzu 841 liquid chromatograph.

(±) - 5 - *Methyl* - (6, *or* 7) - *acetoxybicyclo*[3.2.0]*heptan* - 1 - *one* **6**

A soln of **5** (25.0 g) and vinyl acetate **4** (250 g) in C_6H_6 (90 ml) was irradiated through a Pyrex-filter with a 450-w high pressure mercury lamp (Ushio UM-452) at 4–6° for 60 hr under N_2. The soln was concentrated *in vacuo* and the residue was distilled with a Vigreaux column to give 23.0 g (53.5%) of **6**, b.p. 73–75°/0.3 mm, n_D^{22} 1.4650; ν_{max} 2980 (m), 2890 (m), 1740 (s), 1460 (m), 1420 (m), 1390 (m), 1250 (s), 1175 (m), 1105 (m), 1065 (s), 960 (w), 940 (w), 915 (w) cm^{-1}; δ (60 MHz) 1.15, 1.30, 1.35 (3 H, Me of isomers **6**), 1.97, 1.80 (3 H, AcO of isomers **6**), 2.18–3.00 (7 H, m), 4.65–5.25 (1 H, m); δ (100 MHz, **6** (60 mg) + Eu $(fod)_3$ (80 mg)) 1.60 (0.336 H, s, Me of *endo*-**6b**), 1.84 (1.323 H, s, AcO of *exo*-**6a**), 2.08 (0.924 H, s, Me of *endo*-**6a**), 2.24 (0.417 H, s, *exo*-**6b**), 2.96 (1.338 H, s, AcO of *exo*-**6a**), 3.10 (0.951 H, s, AcO of *endo*-**6a**), 4.04 (0.315 H, s, AcO of *endo*-**6b**), 4.88 (0.396 H, s, AcO of *exo*-**6b**). (Found: C, 65.30; H, 7.70. $C_{10}H_{14}O_3$ requires: C, 65.90; H, 7.75%).

(±) - 2 - *Ethylenedioxy* - 5 - *methyl* - (6, *or* 7) - *acetoxybicyclo*[3.2.0]*heptane* **7**

A soln of **6** (113 g) and *p*-TsOH (1 g) in butanone ethylene ketal (300 g) was heated for 3 hr with removal of the low-boiling butanone through a Vigreaux column. After cooling, the soln was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 126.1 g (91.5%) of **7**, b.p. 93–97°/0.5 mm (analytical sample, 83–85°/0.3 mm), n_D^{20} 1.4620; ν_{max} 2980 (m), 2890 (m), 1750 (s), 1455 (m), 1380 (m), 1365 (m), 1345 (m), 1320 (w), 1250 (s), 1185 (s), 1110 (m), 1060 (m), 1020 (m), 945 (m), 910 (m) cm^{-1}; δ (60 MHz) 1.07, 1.25, 1.62 (3 H, Me of isomers **7**), 1.92, 1.98, 2.08 (3 H, AcO of isomers **7**), 3.80 (4 H, m), 4.60 (1 H, m). (Found: C, 63.89; H, 8.01. $C_{12}H_{18}O_4$ requires: C, 63.68; H, 8.03%)

(±) - 2 - *Ethylenedioxy* - 5 - *methyl* - (6, *or* 7) - *hydroxybicyclo*[3.2.0]*heptane* **8**

Powdered KCN (20 g) was added to a soln of **7** (126.1 g) in 95% EtOH (500 ml) and the mixture was heated under reflux for 20 hr. Then it was concentrated *in vacuo* and extracted with ether. The ether soln was washed with NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 95.4 g (92.9%) of **8**, b.p. 93–103°/0.4 mm, n_D^{20} 1.4780; ν_{max} 3440 (s, OH), 2980 (s), 2900 (s), 1460 (m), 1350 (m), 1180 (m), 1105 (s), 1065 (s), 1020 (s), 945 (m), 910 (m), 890 (m) cm^{-1}; δ (60 MHz) 1.10, 1.15, 1.20, 1.25 (3 H, Me of isomers **8**), 1.50 ~ 2.40 (7 H, m). 3.30 (1 H, br.s, OH), 3.80 (4 H, m).

(±) - 2 - *Ethylenedioxy* - 5 - *methylbicyclo*[3.2.0]*heptan* - 6 - *one* **9** *and* (±) - 2 - *ethylenedioxy* - 5 - *methylbicyclo*[3.2.0]*heptan* - 7 - *one* **10**

A powder of CrO_3–C_5H_5N–HCl (175 g) was gradually added to a stirred and ice-cooled suspension of NaOAc (100 g) in a soln of **8** (94.5 g) in CH_2Cl_2 (1 l). The mixture was stirred for 1 hr at room temp, diluted with ether and filtered through a Florisil column. The column was washed with ether. The combined ether soln was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 72 g (75%) of a mixture of **9** and **10**. This was chromatographed over SiO_2 (Mallinckrodt CC-7, 500 g) in *n*-hexane. Elution with *n*-hexane-ether (9:1) gave **9** (18 g, 78% of total), b.p. 82–92°/0.4 mm (analytical sample, 86–89°/0.1 mm), n_D^{22} 1.4735; ν_{max} 2970(m), 2950 (m), 2900 (m), 2880 (m), 1785 (s), 1455 (m), 1400 (m), 1375 (w), 1340 (w), 1315 (w), 1290 (w), 1245 (m), 1220 (m), 1175 (s), 1120 (s), 1105 (s), 1065 (m), 1045 (m), 1015 (m), 970 (m), 945 (m), 910 (m), 890 (w) cm^{-1}; δ (100 MHz) 1.24 (3 H, s), 1.40 ~ 1.92 (4 H, m), 2.24 (1 H, dd, J_{AC} = 6 Hz, J_{BC} = 10 Hz, H_C), 2.80 (1 H, dd, J_{AC} = 6 Hz, J_{AB} = 20 Hz, H_A), 3.16 (1 H, dd, J_{BC} = 10 Hz, J_{AB} = 20 Hz, H_B) 3.96 (4 H, m); glc (Column, 5% FFAP 1.5 m × 2 mm at 160°; Carrier gas, N_2 1 kg/cm^2): R_t 3.0 min. (Found: C, 65.21; H, 7.71. Calc. for $C_{10}H_{14}O_3$: C, 65.90; H, 7.75%) Further elution with *n*-hexane-ether (9:1) gave 9.5 g of an oil. This was chromatographed again over Al_2O_3 (Woelm neutral alumina, grade II, 50 g) in *n*-hexane. Elution with *n*-hexane-ether (9:1) gave **10** (4.8 g, 22% of total), b.p. 92–100°/1.0 mm, n_D^{22} 1.4810; ν_{max} 2950 (m), 2880 (m), 2840 (m), 1775 (s), 1445 (m), 1390 w), 1375 (w), 1330 (m), 1310 (m), 1260 (m), 1235 (m), 1155 (w), 1130 (w), 1090 (s), 1070 (s), 1030 (s), 1005 (s), 940 (m), 920 (m), 885 (m) cm^{-1}; δ (100 MHz) 1.40 (3 H, s), 1.95 (4 H, m), 2.62 (1 H, dd, J = 4 Hz, J_{AB} = 20 Hz, H_A), 2.80 (1 H, s, H_C), 2.90 (1 H, dd, J = 2 Hz, J_{AB} = 20 Hz, H_B), 3.85 (4 H, m); glc (Column, 5% FFAP 1.5 m × 2 mm at 160°; Carrier gas N_2 1 kg/cm^2): R_t 3.8 min. (Found: C, 65.49; H, 7.71. $C_{10}H_{14}O_3$ requires: C, 65.90; H, 7.75%)

(±) - 2 - *Ethylenedioxy* - 5 - *methyl* - 6 - endo - *hydroxybicyclo*[3.2.0] *heptane* endo-**8a**

A soln of **9** (1.0 g) in dry THF (5 ml) was injected to a stirred and cooled (−60 to −70°) soln of Li (sec-Bu)$_3$BH in THF (1 M, 9 ml, Aldrich) under Ar. The mixture was stirred at −60 to −70° for 15 min and gradually warmed to room temp (1 hr). Subsequently it was ice-cooled and 1 M NaOAc aq (1 ml) was added to the mixture, followed by dropwise addition of 30% H_2O_2 (3.5 ml) at 20–30°. The mixture was concentrated *in vacuo* to remove THF. The residue was extracted with ether. The ether soln was washed with NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 928 mg (92%) of *endo*-**8a**, b.p. 102–110°/0.6 mm, n_D^{22} 1.4830; ν_{max} 3400 (s, OH), 2980 (s), 2960 (s), 1455 (m), 1350 (m), 1105 (s), 1060 (m), 1015 (m), 945 (m), 905 (m) cm^{-1}; δ (60 MHz) 1.10, 1.15 (3 H, Me of isomers **8**), 1.55 ~ 2.50 (6 H, m), 2.95 (1 H, br.s, OH), 3.75 (4 H, m), 4.40 (1 H, m); δ (60 MHz, *endo*-**8a** (60 mg) + Eu $(fod)_3$ (20 mg)) 1.30 (2.67 H, s, Me of *endo*-**8a**), 1.55 (0.33 H, s, Me of *exo*-**8a**). (Found: C, 64.81; H, 8.71. Calc. for $C_{10}H_{16}O_3$: C, 65.18; H, 8.77%) This was contaminated with 11% of *exo*-**8a** as judged by NMR and used for the next step without further purification.

(±) - 2 - *Ethylenedioxy* - 5 - *methyl* - 6 - endo - *acetoxybicyclo*[3.2.0]*heptane* **11**

Ac_2O (28 ml) was added to a ice-cooled soln of *endo*-**8a** (17.0 g) in dry pyridine (56 ml). The mixture was stirred overnight at room temp. poured into ice-water and extracted with ether. The ether soln was washed with $CuSO_4$ soln and water, dried ($MgSO_4$) and concentrated *in vacuo* to give 20.7 g (99%) of **11**, n_D^{20} 1.4658; ν_{max} 2980 (s), 2850 (m), 1750 (s), 1455 (m), 1380 (m), 1365 (m), 1335 (m), 1320 (w), 1290 (w), 1250 (s), 1200 (m), 1180 (m), 1140 (m), 1105 (s), 1075 (m), 1040 (s), 1015 (s), 965 (w), 945 (m), 910 (m), 875 (w) cm^{-1}; δ (100 MHz) 1.24 (3 H, s), 2.00 (3 H, s), 1.40 ~ 2.50 (7 H, m), 3.84 (4 H, m), 4.72 (1 H, seemingly t, J = 6 Hz).

(±) - 5 - *Methyl* - 6 - endo - *acetoxybicyclo*[3.2.0]*heptan* - 2 - *one* endo-**6a**.

A soln of **11** (20.7 g) in 50% AcOH (100 ml) was heated under reflux for 3 hr. After cooling, the mixture was neutralized with powdered $NaHCO_3$ and extracted with ether. The ether soln was washed with NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 12 g (71%) of *endo*-**6a**, b.p. 85–89°/0.5 mm, n_D^{20} 1.4670; ν_{max} 2980 (m), 2850 (m), 1750 (s), 1460 (m), 1390 (m), 1375 (m), 1250 (s), 1190 (m), 1160 (w), 1140 (w), 1120 (w), 1110 (w), 1070 (m), 920 (m) cm^{-1}; δ (100 MHz) 1.36 (3 H, s), 2.04 (3 H, s), 1.40 ~ 2.88 (7 H, m), 4.82 (1 H, seemingly t, J = 6 Hz); δ

(100 MHz, *endo*-**6a** (30 mg) + Eu(fod)$_3$ (40 mg)) 2.08 (2.937 H, s, Me of *endo*-**6a**), 1.84 (0.063 H, s, Me of *exo*-**6a**), 3.10 (2.934 H, s, AcO of *endo*-**6a**), 2.96 (0.066 H, s, AcO of *exo*-**6a**), 6.50 (1 H, seemingly t, J = 6 Hz). (Found: Calc. for C, 65.30; H, 7.76. $C_{10}H_{14}O_3$: C, 65.90; H, 7.75%).

(±) - 2 - *Trimethylsilyloxy* - 5 - *methyl* - 6 - endo - *acetoxybicyclo*[3.2.0]*hept* - 2 - *ene* **12**

n-BuLi (1.52 N in *n*-hexane, 7.6 ml) was added to a stirred and cooled (−50°) soln of *i*-Pr_2NH (1.22 g) in dry THF (10 ml) under Ar. After 10 min, a soln of *endo*-**6a** (2.0 g) in THF (2 ml) was added to the stirred mixture at −50°. After 10 min, chlorotrimethylsilane (2.0 g) was added in one portion and the resulting mixture was gradually warmed to room temp (2 hr). The mixture was diluted with ether and filtered through Celite. The filtrate was concentrated *in vacuo*. The residue was triturated with *n*-hexane and filtered through Celite. The filtrate was concentrated *in vacuo* to give 2.54 g (91.3%) of **12**, n_D^{20} 1.4650; ν_{max} 3050 (w), 2950 (s), 2840 m), 1740 (s), 1635 (m), 1450 (m), 1380 (m), 1360 (m), 1340 (m), 1310 (m), 1250 (s), 1210 (s), 1190 (m), 1140 (m), 1100 (m), 1065 (m), 1000 (m), 975 (m), 920 (m), 840 (s) cm^{-1}; δ (60 MHz) 0.18 (9 H, s, OTMS), 1.27 (3 H, s), 1.98 (3 H, s), 1.70 ~ 2.80 (5 H, m), 4.55 (1 H, m), 4.70 (1 H, m).

(±) - 4 - *Acetoxy* - 2 - *methoxycarbonyl* - 1 - *methylcyclobutane* - 1 - *acetaldehyde ethylene acetal* **16**

Ozonised O was introduced to a soln of **12** (2.54 g) in CH_2Cl_2 (25 ml) at −66 to −64° for 10 min. The soln was treated with Ph_3P (2.0 g) and then left to stand overnight at room temp under Ar. After addition of AcOH (5 drops) the mixture was stirred for 3 hr, esterified with CH_2N_2 and concentrated *in vacuo*. The residual oil (4.2 g) was dissolved in CH_2Cl_2 (10 ml). Methyl ethylene orthoformate (6.0 g) and *p*-TsOH (50 mg) was added to the soln and the mixture was left to stand for 2 days at room temp. The CH_2Cl_2 soln was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil (5.2 g). This was chromatographed over SiO_2 (Mallinckrodt CC-7, 40 g) in *n*-hexane. Elution with *n*-hexane gave unreacted Ph_3P (600 mg). Further elution with *n*-hexane-ether (9:1) gave 293 mg (10.8%) of **16**, n_D^{20} 1.4765; ν_{max} 2950 (m), 1735 (s), 1450 (m), 1380 (m), 1240 (s), 1200 (m), 1180 (m), 1040 (m), 1130 (m), 1100 (m), 1075 (m), 1050 (m), 985 (m), 945 (m), 910 (m), 850 (m) cm^{-1}; δ (60 MHz) 1.35 (3 H, s), 2.00 (3 H, s), 1.50 ~ 2.80 (5 H, m), 3.60 (3 H, s), 3.70 ~ 4.00 (4 H, m), 4.20 (1 H, t, J = 6 Hz), 4.70 (1 H, m).

(±) - 3,3,7 - *Trimethyl* - 2,9 - *dioxatricyclo*[4.2.1.0^{4,7}]*nonane* (±) - **2**

A soln of **16** (290 mg) in dry ether (1 ml) was gradually added to a stirred and ice-cooled soln of MeMgI (from 0.3 g of Mg and 2.5 g of MeI) in ether (4 ml). The mixture was stirred for 2 hr at room temp, poured into ice–10% HCl and extracted with *n*-pentane. The *n*-pentane soln was successively washed with $NaHCO_3$ aq, NaCl aq, $Na_2S_2O_3$ aq and water, dried ($MgSO_4$–K_2CO_3) and concentrated under atm press. The residue was distilled to give 47 mg (28%) of (±)-**2**, b.p. 120–130° (bath temp)/60 mm, n_D^{20} 1.4672; ν_{max} (CCl_4) 2960 (s), 2920 (s), 2850 (m), 1445 (m), 1385 (m), 1370 (m), 1360 (m), 1350 (w), 1330 (m), 1305 (w), 1260 (w), 1240 (w), 1215 (m), 1200 (m), 1180 (m), 1160 (w), 1150 (s), 1120 (s), 1100 (m), 1050 (s), 1040 (w), 1020 (m), 1000 (m), 990 (w), 980 (w), 950 (w), 940 (s), 920 (w), 910 (s), 895 (s), 850 (w) cm^{-1}; δ (100 MHz, CCl_4) 1.06 (3 H, s), 1.20 (3 H, s), 1.37 (3 H, s), 1.50 ~ 2.60 (5 H, m), 3.88 (1 H, t, J = 6 Hz, CHOR), 5.24 (1 H, d, J = 6 Hz, CH (OR) OR'); MS: *m/e* 43.0212 (C_3H_7O, 100%), 55.0556 (C_4H_7, 83%), 69.0705 (C_5H_9, 90%), 81.0708 (C_6H_9, 69%), 83.0497 (C_5H_7O, 56%), 95.0070 (C_7H_{11}, 46%), 107.0846 (C_8H_{11}, 37%), 109.0636 (C_7H_9O, 82%). 139.1120 ($C_9H_{15}O$, 15%), 153.0905 ($C_9H_{13}O_2$, 8%), 168.1123 (Calc. for $C_{10}H_{16}O_2$: 168.1150, 1%, M$^+$).

(±) - *Ethylendioxy* - 5 - *methyl* - 7 - endo - *hydroxybicyclo*[3.2.0]*heptane* endo-**8b**

This was prepared in the similar manner as described for *endo*-**8a**, starting from **10** (3.8 g) and Li(sec-Bu)$_3$BH (36 ml) to give 3.8 g (98.5%) of *endo*-**8b** as an unstable oil, n_D^{20} 1.4785; ν_{max} 3480 (s, OH), 2940 (s), 2880 (s), 2760 (s), 1450 (m), 1350 (m), 1100 (s), 1010 (s) cm^{-1}; δ (60 MHz) 1.18 (3 H, s), 1.35 ~ 2.62 (6 H, m), 3.50 (1 H, br.s, OH), 3.88 (4 H, m), 4.25 (1 H, seemingly q, J = 6 Hz); δ (60 MHz, after 20 hr in CCl_4) ~1.10, ~1.18, ~1.24, ~1.75, ~2.42, ~3.80, ~9.60 (CHO).

(±) - 2 - *Ethylenedioxy* - 5 - *methyl* - 7 - endo - *acetoxybicyclo*[3.2.0]*heptane* **13**

Acetic anhydride (10 ml) was added to an ice-cooled soln of *endo*-**8b** (3.8 g) in dry pyridine (10 ml) with stirring. Subsequent treatments as described for **11** gave 3.8 g (82.6%) of **13**, n_D^{20} 1.4620; ν_{max} 2940 (s), 2860 (s), 1735 (s), 1440 (m), 1375 (m), 1355 (m), 1340 (m), 1320 (m), 1250 (s), 1170 (m), 1135 (m), 1105 (s), 1060 (m), 1020 (m), 1000 (m), 945 (m) cm^{-1}. This was employed for the next step without further purification.

(±) - 5 - *Methyl* - 7 - endo - *acetoxybicyclo*[3.2.0]*heptan* - 2 - *one* endo-**6b**

This was prepared in the similar manner as described for *endo*-**6a**, starting from **13** (3.8 g) to give 2.54 g (83%) of *endo*-**6b**, b.p. 90–102°/1.2 mm, n_D^{20} 1.4678; ν_{max} 2920 (m), 2840 (m), 1735 (s), 1440 (w), 1410 (w), 1375 (m), 1240 (s), 1155 (m), 1105 (m), 1100 (m), 1045 (s), 935 (m) cm^{-1}; δ (100 MHz) 1.36 (3 H, s), 1.90 (3 H, s), 1.60 ~ 2.70 (7 H, m), 5.08 (1 H, seemingly q, J = 6 Hz); δ (100 MHz, *endo*-**6b** (50 mg) + Eu(fod)$_3$ (72 mg)) 1.60 (2.985 H, s, Me of *endo*-**6b**), 2.08 (0.015 H, s, Me of *exo*-**6b**), 3.78 (2.985 H, s, AcO of *endo*-**6b**), 4.60 (0.015 H, s, AcO of *exo*-**6b**), 7.48 (1 H, seemingly q, J = 6 Hz). (Found: C, 65.75; H, 7.76. $C_{10}H_{14}O_3$ requires: C, 65.90; H, 7.75%)

(±) - *Trimethylsilyloxy* - 5 - *methyl* - 7 - endo - *acetoxybicyclo*[3.2.0]*hept* - 2 - *ene* **14**

n-BuLi (1.52 N in *n*-hexane, 8.4 ml) was added to a stirred and cooled (−50°) soln of *i*-Pr_2NH (1.35 g) in dry THF (10 ml) under Ar. After 20 min, a soln of *endo*-**6b** (2.2 g) in THF (2 ml) was added to the stirred mixture at −50°. After 10 min, chlorotrimethylsilane (2.5 g) was added in one portion to the mixture. The mixture was warmed gradually to room temp (1 hr). Subsequent work up as described for **12** gave 3.0 g (97.7%) of **14**, n_D^{20} 1.4710; ν_{max} 3060 (w), 2950 (s), 2840 (m), 1735 (s), 1630 (m), 1450 (m), 1375 (m), 1360 (m), 1315 (m), 1255 (s), 1205 (m), 1170 (m), 1130 (m), 1090 (m), 1055 (m), 990 (m), 880 (m), 840 (s) cm^{-1}; δ (60 MHz) 0.20 (9 H, s, OTMS), 1.20 (3 H, s), 2.00 (3 H, s), 1.50 ~ 2.50 (5 H, m), 4.70 (1 H, m), 5.20 (1 H, m).

(±) - 3 - *Acetoxy* - 2 - *methoxycarbonyl* - 1 - *methylcyclobutane* - 1 - *acetaldehyde ethylene acetal* **18**

This was prepared in the similar manner as described for **16**, starting from 3.0 g of **14**. The crude product was chromatographed over SiO_2 (Mallinckrodt CC-7, 50 g) in *n*-hexane. Elution with *n*-hexane-ether (9:1) gave 350 mg (14%) of **18**, n_D^{20} 1.4700; ν_{max} 2950 (s), 1740 (a), 1440 (m), 1380 (m), 1250 (s), 1180 (s), 1160 (s), 1125 (s), 1090 (s), 1050 (s), 950 (m) cm^{-1}; δ (60 MHz) 1.30 (3 H, s), 2.00 3 H, s), 1.60 ~ 2.75 (5 H, m), 3.65 (3 H, s), 3.80 (4 H, m), 4.20 (1 H, m), 5.00 (1 H, m), 8.00 (impurity).

(±) - 3,3,7 - *Trimethyl* - 2,9 - *dioxatricyclo*[3.3.1.0^{4,7}]*nonane* (*lineatin*) (±)-**1**

A soln of **18** (300 mg) in dry ether (1 ml) was gradually added to a stirred and ice-cooled soln of MeMgI (from 0.5 g of Mg and 4.0 g of MeI) in ether (15 ml). The mixture was stirred for 2 hr at room temp, poured into ice-10%-HCl and extracted with *n*-pentane. The *n*-pentane layer was separated and the aq layer was extracted with *n*-pentane. The combined *n*-pentane soln was successively washed with $NaHCO_3$ aq, NaCl aq, $Na_2S_2O_3$ aq and water, dried ($MgSO_4$–K_2CO_3) and concentrated under atm press to give a crude oil (*ca* 100 mg). This was chromatographed over Al_2O_3 (Woelm neutral alumina, grade II, 1 g) in *n*-pentane. Elution with *n*-pentane-ether (9:1) gave 8 mg of pure (±)-**1**, ν_{max} (CCl_4) 2940 (s), 2900 (s), 2850 (m), 1465 (m), 1450 (m), 1380 (m), 1365 (m), 1340 (w), 1315 (m), 1240 (m), 1225 (m), 1205 (m), 1185 (m), 1170 (s), 1125 (s), 1100 (m), 1075 (m), 1015 (w), 995 (m), 965 (s), 920 (w), 900 (s), 830 (w) cm^{-1}; δ (100 MHz, CCl_4) 1.09 (3 H, s), 1.14 (6 H, s), 1.50 ~ 2.40 (5 H, m), 4.34 (1 H, t, J = 6 Hz, CHOR), 4.86 (1 H, d, J = 6 Hz, CH (OR) OR'); MS: *m/e* 168 (M$^+$), 153

(M^+-Me), 140, 125, 111, 109, 107, 96, 85 (base peak), 83, 55, 43. These spectral data were identical with those of the literature.[1]

2,4,4 - *Trimethylcyclopent* - 1 - *yl acetate* **23**

Ac_2O (242.5 ml) and $HClO_4$ (0.36 ml) was added to a soln of **22** (65 g) in CCl_4 (600 ml). The mixture was stirred at room temp for 2 hr, poured into satd $NaHCO_3$ (300 ml) and neutralised with powdered $NaHCO_3$. The resulting mixture was filtered through Celite. The CCl_4 layer was separated and the aq layer was extracted with *n*-pentane. The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 70.6 g (81%) of **23**, b.p. 73–75°/17 mm, n_D^{20} 1.4400; ν_{max} 1760 (s), 1750 (s), 1700 (m), 1235 (s), 1215 (m) cm^{-1}; δ (60 MHz) 1.10 (6 H, s), 1.45 (3 H, s), 2.05 (3 H, s, AcO), 1.90 ~ 2.30 (4 H, m), (Found: C, 72.34; H, 9.34., Calc. for $C_{10}H_{16}O_2$: C, 71.38; H, 9.61%)

2,4,4 - *Trimethylcyclopent* - 2 - *en* - 1 - *one* **19**

(a) A soln of **23** (70.6 g) in THF (70 ml) was added to a soln of N-bromosuccinimide (111.5 g) in THF (300 ml) and water (75 ml) at 15–20°. The mixture was left to stand overnight at room temp. The mixture was concentrated *in vacuo* to remove THF and extracted with ether. The ether soln was washed with $Na_2S_2O_3$ aq and water, dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil of **24** (*ca* 120 g). This was dissolved in pyridine (100 ml) and Li_2CO_3 (30 g) was added. The mixture was heated at 90–100° for 1 hr. After cooling, the mixture was poured into ice-HCl and extracted with ether. The ether soln was successively washed with water, $NaHCO_3$ aq and water, dried $MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 47 g (90.4%) of **19**, b.p. 63–65°/20 mm (lit.[17] 60°/20 mm), n_D^{20} 1.4635; ν_{max} 1705 (s), 1635 (m) cm^{-1}; δ (60 MHz) 1.18 (6 H, s), 1.68 (3 H, d, J = 1 Hz), 2.15 (2 H, s), 6.98 (1 H, d, J = 1 Hz).

(b) Isobutyl methacrylate (30 g) was added to polyphosphoric acid (116%, 250 g) at 100° under Ar. After stirring for 10 min, the mixture was poured into ice-water (1 l), satd with NH_4Cl and extracted with ether. The ether soln was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 12 g (45.6%) of **19**, b.p. 63–65°, n_D^{20} 1.4626. Its IR and NMR spectra were identical with those of method (a).

(±) - 1,4,4 - *Trimethyl* - (6, *or* 7) - *acetoxybicyclo*[3.2.0]*heptan* - 2 - *one* **26a** + **26b**

A soln of **19** (25 g) and vinyl acetate (250 ml) in C_6H_6 (90 ml) was irradiated through a Pyrex-filter with a 450 W high pressure mercury lamp (Ushio UM-452) at 4–6° for 60 hr under N_2. The soln was concentrated *in vacuo* and the residue was fractionally distilled with a Vigreaux column to give 14 g of recovered **19**, 1.2 g of a mixture of **19**, **26a** and **26b**, and 11 g of a mixture of **26a** and **26b**, b.p. 92–98°/0.5 mm. The photo-adducts were analyzed by glc (Column, 5% FFAP 1.5 m × 2 mm at 100–220°, temp gradient 16°/min; Carrier gas, N_2 1 kg/cm²): R_t 5.2 (55.4%), 5.5 (10.4%), 5.8 (3.6%), 6.1 (24.4%), 7.1 (6.2%) min. In its NMR spectrum the mixture exhibited signals due to CHOAc at ~4.00, ~4.60, ~4.80 and ~5.20, a signal due to CHO at 9.50. For analysis, this was further purified by preparative tlc (Merck Kieselgel Art 5717, *n*-hexane-acetone (4:1)), b.p. 86°/0.2 mm, n_D^{20} 1.4620; ν_{max} 2950 s), 2845 (m), 1735 (s), 1450 (m), 1370 (m), 1250 (s), 1050 (m) cm^{-1}; δ (100 MHz) 0.94 ~ 1.24 (9 H, m), 1.72 ~ 2.92 (5 H, m), 4.60 (0.4 H, seemingly t, CHOAc of **26a**), 4.90 (0.4 H, seemingly q, CHOAc of **26b**), 5.30 (0.2 H, seemingly q, CHOAc of **26b**). (Found: C, 68.27; H, 8.71. Calc. for $C_{12}H_{18}O_3$: C, 68.53; H, 8.64%)

(±) - 1,4,4 - *Trimethyl* - 3 - *oximino* - 6 - exo - *hydroxybicyclo*[3.2.0]*heptan* - 2 - *one* **28**

A soln of the photo-adducts **26a** and **26b** (9.0 g) in C_6H_6 (20 ml) was added to a stirred and ice-cooled soln of *t*-AmOK (10.5 g, from 3.0 g of K and 50 ml of *t*-AmOH) in C_6H_6 (100 ml). After stirring for 30 min, *i*-AmONO (4.5 g) was added to the mixture. The mixture was stirred at room temp for 36 hr and acidified with 1 N HCl.

The benzene layer was separated, washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil (9.38 g). This was chromatographed over SiO_2 (Mallinckrodt CC-7 (140 g), in *n*-hexane. Elution with *n*-hexane gave 1.6 g of isoamyl acetate. Elution with chloroform (150 ml) gave a crystalline *syn*-**28** (103 mg), m.p. 115–117°; ν_{max} ($CHCl_3$) 3550 (m), 3400 (m), 2955 (s), 2920 (m), 2850 (m), 1685 (s), 1565 (m), 1465 (m), 1450 (m), 1360 (m), 1300 (m), 1210 (m), 1115 (m), 1045 (m), 1030 (m), 955 (s) cm^{-1}; δ (100 MHz, CD_3COCD_3) 1.12 (3 H, s), 1.20 (3 H, s), 1.28 (3 H, s), 1.86 (1 H, dd, J = 8 Hz, J = 14 Hz), 2.20 (1 H, d, J = 6 Hz), 2.36 (1 H, dd, J = 6 Hz, J = 8 Hz), 3.84 (2 H, m); δ (100 MHz, *syn*-**28** (70 mg) + Eu(fod)$_3$ (20 mg) in CD_3COCD_3) 1.12 (3 H, s), 1.22 (3 H, s), 1.32 (3 H, s), 1.92 (1 H, dd, J = 8 Hz, J = 14 Hz). 2.24 (1 H, d, J = 6 Hz), 3.88 (2 H, m), 4.40 (2 H, bs, OH). (Found: C, 60.90; H, 8.22; N, 6.81. Calc. for $C_{10}H_{15}NO_3$: C, 60.88; H, 7.68; N, 7.04%) Further elution with chloroform (600 ml) gave a crystalline mixture of *syn* - and *anti*-**28** (930 mg). Further elution with chloroform (100 ml) gave a crystalline *anti*-**28** (60 mg), m.p. 137–140°; ν_{max} ($CHCl_3$) 3300 (s), 2950 (s), 2900 (s), 2845 (m), 1720 (s), 1620 (m), 1450 (m), 1370 (m), 1290 (m), 1220 (m), 1185 (m), 1115 (m), 1050 (m), 950 (s), 755 (s) cm^{-1}; δ (100 MHz, CD_3COCD_3), 1.10 (3 H, s), 1.20 (3 H, s), 1.28 (3 H, s), 1.88 (1 H, dd, J = 8 Hz, J = 14 Hz), 2.20 (1 H, d, J = 6 Hz), 2.36 (1 H, dd, J = 8 Hz, J = 14 Hz), 3.86 (1 H, dd, J = 6 Hz, J = 8 Hz), 4.15 (1 H, bs, OH), 12.40 (1 H, bs, NOH). The total yield of **28** was 1093 mg (30%). Both *syn*- and *anti*-isomers were used for the next step as the mixture.

(±) - 1,4,4 - *Trimethyl* - 3 - *oximino* - 6 - exo - *hydroxybicyclo*[3.2.0]*heptane* **29**

A mixture of **28** (2050 mg), N_2H_4 (80%, 0.7 ml), KOH (750 mg) and ethylene glycol (25 ml) was heated at 150° for 4 hr under Ar. The mixture was allowed to cool, diluted with water, acidified with 1 N HCl and extracted with CH_2Cl_2. The CH_2Cl_2 soln was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 970 mg (52%) of crystalline **29**, m.p. 130–133°; ν_{max} ($CHCl_3$) 3570 (m), 3260 (m), 2940 (s), 2900 (s), 1635 (m), 1440 (m), 1375 (m), 1360 (m), 1295 (w), 1210 (m), 1120 (m), 1085 (m), 1040 (m), 930 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.12 (3 H, s), 1.22 (3 H, s), 1.38 (3 H, s), 1.80 ~ 2.70 (5 H, m), 3.80 (1 H, m); MS: *m/e* 183 (M^+).

(±) - 1,4,4 - *Trimethyl* - 6 - exo - *hydroxybicyclo*[3.2.0]*heptane* (±)-**30**

A mixture of **29** (600 mg), dimethoxyethane (10 ml), water (5 ml) and $TiCl_3$ (16% aq, 6 ml) was heated at 50–60° for 30 min. The cooled mixture was diluted with water and extracted with CH_2Cl_2. The CH_2Cl_2 soln was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil (425 mg). This was chromatographed over SiO_2 (Mallinckrodt CC-7, 10 g) in *n*-hexane. Elution with *n*-hexane-ether (1:1) gave 305 mg (55.5%) of (±)-**30** as an oil, n_D^{20} 1.4787, which solidified in a freezer to give a waxy solid, m.p. 52–53°; ν_{max} 3400 (m), 2940 (s), 2900 (s), 2845 (m), 1730 (s), 1460 (m), 1400 (w), 1375 (m), 1360 (w), 1330 (w), 1300 (w), 1265 (w), 1230 (w), 1205 (m), 1105 (s), 1050 (m), 1005 (m), 955 (m), 910 (w), 840 (w), 790 (w) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.98 (3 H, s), 1.04 (3 H, s), 1.80 (1 H, dd, J = 8 Hz, J = 12 Hz), 2.12 (1 H, d, J = 6 Hz), 2.14 (1 H, d, J = 20 Hz), 2.28 (1 H, m), 2.42 (1 H, d, J = 20 Hz), 2.84 (1 H, bs, OH), 3.76 (1 H, q, J = 6 Hz); MS: *m/e* 168 (M^+). Elution with ether gave 52 mg (8%) of **31**, m.p. 60–62°; ν_{max} ($CHCl_3$) 3450 (s), 1660 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.05 (6 H, s), 1.35 (3 H, s), 2.10 ~ 2.60 (5 H, m), 4.60 ~ 4.80 (3 H, m).

Optical resolution of (±)-**30**

(a) *Separation of a diastereomeric mixture of the carbamates* **36** *and* **37**. A mixture of (±)-**30** (900 mg), (*S*)-(+)-**35** (1.2 g) and dry pyridine (5 ml) was heated at 80–90° for 10 hr. The cooled soln was mixed with ether and 10% HCl. The ether layer was separated, washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give a diastereomeric mixture of **36** and **37** (1.68 g, 85.9%). This was chromatographed over SiO_2 (Merck Lobar column size C, 37 mm × 440 mm) in CH_2Cl_2–AcOEt (10:1). The eluent was monitored at 280–315 nm by JASCO UVIDEC 100-II photometer. The unresolved fractions were chromatographed

again by using a Merck Lobar column size B, 25 mm × 370 mm. The first major fraction to be eluted was **36** (195 mg), m.p. 47–48°, $[\alpha]_D^{23}$ −8.0° (*c* = 0.5, EtOH); ν_{max} ($CHCl_3$) 3430 (m), 1730 (s), 1715 (s), 1500 (s), 1230 (m), 1065 (s), 905 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.00 (3 H, s), 1.05 (3 H, s), 1.35 (3 H, s), 1.55 (3 H, d, J = 6 Hz), 5.50 ~ 5.80 (1 H, m), 7.20 ~ 8.25 (7 H, m). (Found: C, 74.95; H, 7.41; N, 3.72. Calc. for $C_{23}H_{27}NO_3$: C, 75.57; H, 7.41; N, 3.83%) This was contaminated with 7.75% of **37** as determined by hplc analysis (Column, μ-Porasil 7.8 mm × 30 cm at room temp, CH_2Cl_2–AcOEt (20:1); Flow rate, 2 ml/min; Pressure, 25 kg/cm^2): R_t 34.5 min (92.25%), 40.0 min (7.75%). The second major fraction to be eluted was **37** (210 mg), m.p. 111–112°, $[\alpha]_D^{23}$ + 23.5° (*c* = 1.0, EtOH); ν_{max} ($CHCl_3$) 3430 (m), 1730 (m), 1715 (s), 1500 (s), 1230 (s), 1065 (s), 905 (s) cm^{-1}; δ (60 MHz, $CDCl_3$) 0.95 (6 H, bs), 1.35 (3 H, s), 1.55 (3 H, d, J = 6 Hz), 2.00 ~ 2.50 (5 H, m), 4.65 (1 H, q, J = 6 Hz), 5.05 (1 H, d, J = 6 Hz), 5.50 ~ 5.80 (1 H, m), 7.20 ~ 8.25 (7 H, m). (Found: C, 74.46: H, 7.38; N, 3.66. Calc. for $C_{23}H_{27}NO_3$: C, 75.57; H, 7.41; N, 3.83%) This was contaminated with 6.00% of **36** as determined by hplc analysis in the same conditions as described above for **36**: R_t 34.5 min (6.00%), 40.0 min (94.0%).

(b) *Conversion of* **36** (**37**) *to* (1R, 5S, 6S) - (−) - **30**[(1S, 5R, 6R) - (+) - **30**]. The carbamate **36** (195 mg) was dissolved in 3% EtONa–EtOH and the mixture was heated under reflux for 15 min. The cooled soln was diluted with water, neutralised with dil HCl aq and extracted with ether. The ether soln was washed with NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil. This was purified by preparative tlc (Merck Kieselgel 60, Art 5717, *n*-hexane-acetone (4:1)). The band between R_f 0.2 and 0.3 was collected and eluted with ether. The ether was evaporated to give 70 mg (78%) of (−)-**30**, m.p. 55–56°, $[\alpha]_D^{22}$-21.7° (*c* = 1.16, acetone), CD (*c* = 0.1, MeOH) $[\theta]_{292}^{26}$-1562. The optical purity of (−)-**30** was estimated by hplc analysis of the carbamate **36** to be 84.5%. Its IR spectrum was identical with that of the racemate **30**.

A similar hydrolysis of the carbamate **37** (210 mg) gave 90 mg (93.1%) of (+)-**30**, m.p. 55–56°, $[\alpha]_D^{22}$ + 23.6° (*c* = 0.94, acetone), CD (*c* = 0.1, MeOH) $[\theta]_{292}^{26}$ + 1613. The optical purity of (+)-**30** was estimated by hplc analysis of the carbamate **37** to be 88.0%. Its IR spectrum was identical with that of the racemate.

1,5,5 - *Trimethyl* - 7 - exo - *hydroxy* - 4 - *oxabicyclo*[4.2.0]*octan* - 3 - *one* **32**

(a) *Racemate. m*-Chloroperbenzoic acid (770 mg) and powdered $NaHCO_3$ (480 mg) was added to a soln of (±)-**30** (400 mg) in CH_2Cl_2 (8 ml) and the mixture was stirred overnight at room temp. The reaction was quenched with 10% $Na_2S_2O_3$ aq (10 ml) and the mixture was stirred for 30 min. The CH_2Cl_2 layer was separated and the aq layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 layer was washed with $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 415 mg (94.7%) of (±)-**32**, n_D^{20} 1.4845; ν_{max} 3380 (s), 2950 (s), 2910 (s), 2840 (m), 1720 (s), 1465 (m), 1450 (m), 1420 (m), 1390 (m), 1370 (m), 1295 (s), 1260 (m), 1235 (m), 1210 (s), 1155 (s), 1105 (s), 1050 (m), 1020 (m), 990 (s), 985 (m), 950 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.40 (9 H, bs), 1.90 ~ 2.95 (5 H, m), 4.20 (1 H, q, J = 8 Hz), 4.70 (1 H, bs, OH); MS: *m/e* 169 (M^+-Me), 166 (M^+-H_2O).

(b) (1R, 6S, 7S)-(−)-**32**. In the similar manner, 60 mg of (−)-**30** gave 52 mg of crude (−)-**32**, whose IR spectrum was identical with that of the racemate. This was employed for the next step without further purification.

(c) (1S, 6R, 7R)-(+)-**32**. In the similar manner, 80 mg of (+)-**30** gave 71 mg of crude (+)-**32**, whose IR spectrum was identical with that of the racemate. This was employed for the next step without further purification.

1,5,5 - *Trimethyl* - 4 - *oxabicyclo*[4.2.0]*octane* - 3,7 - *dione* **33**

(a) *Racemate.* Jones CrO_3 (0.6 ml) was added to a soln of (±)-**32** (410 mg) in acetone (10 ml) at 0–4°. After stirring for 10 min, a few drops of *i*-PrOH was added to the mixture to destroy excess of the oxidant. The mixture was diluted with CH_2Cl_2 (10 ml) and water (10 ml). The CH_2Cl_2 layer was separated and the aq layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 layer was washed with NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 342 mg (84.0%) of (±)-**33**, n_D^{20} 1.4837; ν_{max} 2950 (m), 2900 (m), 2840 (m), 1775 (s), 1730 (s), 1450 (m), 1420 (m), 1385 (m), 1370 (m), 1330 (m), 1290 (s), 1255 (m), 1215 (m), 1190 (m), 1135 (s), 1115 (m), 1110 (m), 1060 (m), 1035 (m), 980 (m), 940 (m), 810 (w) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.46 (3 H, s), 1.58 (6 H, s). 2.40 ~ 3.24 (5 H, m); MS: *m/e* 182 (M^+).

(b) (1R, 6R)-(−)-**33**. In the similar manner, 52 mg of (−)-**32** gave 40 mg of (−)-**33**, $[\alpha]_D^{23}$ −45.2° (*c* = 0.8, acetone), whose IR spectrum was identical with that of the racemate. This was employed for the next step without further purification.

(c) (1S, 6S)-(+)-**33**. In the similar manner, 71 mg of (+)-**32** gave 57 mg of (+)-**33**, $[\alpha]_D^{23}$ + 49.1° (*c* = 1.14, acetone), whose IR spectrum was identical with that of the racemate. This was employed for the next step without further purification.

3,3,7 - *Trimethyl* - 2,9 - *dioxatricyclo*[3.3.1.$0^{4,7}$]*nonane* (*lineatin*) **1**

(a) *Racemate.* Diisobutylaluminium hydride (25% in *n*-hexane, 2.1 ml) was injected to a stirred and cooled (−70 to −50°) soln of (±)-**33** (300 mg) in dry ether (3 ml). After stirring for 40 min, 1 N HCl (5 ml) was added to the mixture. The mixture was gradually warmed to room temp (1 hr), followed by addition of 6 N HCl (0.6 ml) and the stirring was continued for 1 hr at room temp. The mixture was diluted with *n*-pentane. The *n*-pentane layer was successively washed with NaCl aq, $NaHCO_3$ aq and NaCl aq, dried ($MgSO_4$) and concentrated under atm press to give a crude oil (110 mg). This was distilled to give 56 mg of pure (±)-**1**, b.p. 120–130° (bath temp)/60 mm, n_D^{20} 1.4625; MS: *m/e* 43.0123 (C_2H_3O, 42%), 55.0563 (C_4H_7, 66%), 83.0516 (C_5H_7O, 48%), 85.0682 (C_5H_7O, 100%), 96.0583 (C_6H_8O, 38%), 107.0854 (C_8H_{11}, 35%), 111.0440 ($C_6H_7O_2$, 36%), 125.0967 ($C_8H_{13}O$, 25%), 140.1184 ($C_9H_{16}O$, 4%), 153. 0905 ($C_9H_{13}O_2$, 3%), 168.1183 (Calc. for $C_{10}H_{16}O_2$: 168.1150, 2%, M^+). Its IR and NMR spectra were identical with those of previously synthesized one.

(b) (1R, 4S, 5R, 7R)-(−)-**1**. In the similar manner, (−)-**33** (40 mg) was treated with *i*-Bu_2AlH (0.35 ml). Subsequent work up as described for the racemate gave a crude oil, which was chromatographed over Al_2O_3 (Woelm neutral alumina, grade II, 400 mg) in *n*-pentane. Elution with *n*-pentane-ether (19:1) gave 0.5 mg of (−)-**1**, $[\alpha]_D^{22}$ − 40° (*c* = 0.05, *n*-pentane); ORD (qualitative, *n*-pentane), (−)-plain curve at 230 nm–350 nm, whose MS was identical with that of the racemate.

(c) (1S, 4R, 5S, 7S)-(+)-**1**. In the similar manner, (+)-**33** (54 mg) was treated with *i*-Bu_2AlH (0.4 ml). Subsequent work up as described for the racemate gave a crude oil, which was chromatographed over Al_2O_3 (Woelm neutral alumina, grade II, 650 mg) in *n*-pentane. Elution with *n*-pentane-ether (19:1) gave 2 mg of (+)-**1**, $[\alpha]_D^{22}$ + 36° (*c* = 0.2, *n*-pentane); ORD (qualitative, *n*-pentane), (+)-plain curve at 230–350 nm, whose MS was identical with that of the racemate.

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