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Diterpene Imines. The Preparation of 2-Azalauren-1-ene and the Facile Autoxidation of 6-Azadihydrorimuene

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Abstract

2-Azalauren-1-ene (2) has been synthesized from keto acid (5), but attempts to generate its C15 epimer (19) have produced only (2). Model studies of imine production by treatment of a rimuene-derived keto acid (3) with iodosylbenzene/formic acid have produced a hydroxy imine (11), a conjugated imine (13), and a keto lactam (12) which has a ten-membered ring. An X-ray crystallographic study which proves the structure of (12) is described. Data in support of the intermediacy of imine (7) (6-azadihydrorimuene) in the production of (11), (12) and (13) have been obtained.

Introduction

The pentamethyl [5.5.5.7] fenestrane skeleton which is to be found in lauren-1-ene (1), presents a unique combination of compactness and chirality. In view of the important pharmaceutical applications which have been developed for derivatives of adamantane (for example, see ref. 1), another highly compact entity, coupled with the diverse biological activities found for nitrogen-containing natural products in general, it seemed appropriate to develop syntheses of azalaurenanes. Our initial target was the imine derivative 2-azalauren-1-ene (2), a substance which has potential for further derivatization.

Keto acid (3), a substance which is readily available from the diterpene rimuene (4),[2] was chosen as a model compound for our work. The laurenene chemistry was to be performed on the epimeric keto acids (5) and (6).[3]

Derivatives of Rimuene

Our goal was the imine (7) which we proposed to form from keto amide (8) through keto amine (9). Conversion of keto acid (3) into the keto amide (8) was achieved in good yield by way of keto acid anhydride (10), produced upon the dropwise addition of ethyl chloroformate to a solution of (3) and triethylamine at 0°. The i.r. spectrum of (8) showed the characteristic absorption bands of the amide at 3344, 3168, 1666 and 1615 cm^{-1}, and of the ketone at 1699 cm^{-1}.

[1] Wishnok, J. S., *J. Chem. Educ.*, 1973, 780.
[2] Corbett, R. E., and Wyllie, S. G., *J. Chem. Soc. C*, 1966, 1737.
[3] Corbett, R. E., Lauren, D. R., and Weavers, R. T., *J. Chem. Soc., Perkin Trans. 1*, 1979, 1774.

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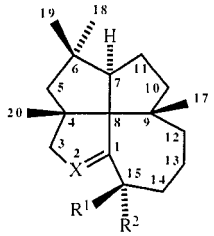
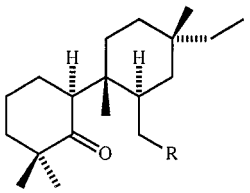
It has been reported[4] that a solution of iodosylbenzene and formic acid in aqueous acetonitrile causes rearrangement of aliphatic amides to amines (as formate salts) under very mild conditions. The reaction proceeds in one step and in high yield. It was proposed that the formic acid catalyses attack of water on the intermediate isocyanate, and protonates the resulting amine. As a result the amine cannot act as a nucleophile. Only primary amides undergo the reaction. Treatment of (8) for 16 h at room temperature under these conditions, followed by extraction into aqueous acid, basification and ether extraction, gave a white crystalline product which was shown by analysis (g.l.c. and ^1H and ^{13}C n.m.r.) to be a complex mixture. G.l.c. analysis of the reaction mixture upon isolation revealed the presence of an intermediate ($t_{1/2}$ *c.* 1 h) which quickly converted into products with longer retention times.

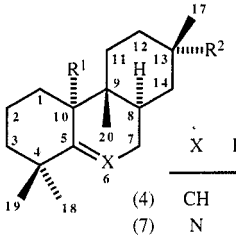
Radial chromatography of the reaction mixture enabled the isolation of three new compounds; hydroxy imine (11) and keto lactam (12) as the major products, and keto imine (13) as a minor product.*



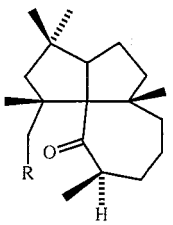
	X	R^1	R^2
(1)	CH	Me	H
(2)	N	Me	H
(19)	N	H	Me
(23)	CH	H	Me



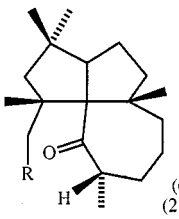
(3) R = COOH
(8) R = $CONH_2$
(9) R = NH_2
(10) R = COOCOOEt



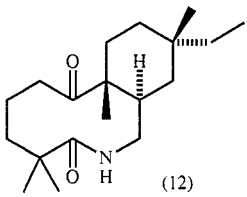
	X	R^1	R^2
(4)	CH	H	$CH=CH_2$
(7)	N	H	Et
(11)	N	OH	Et



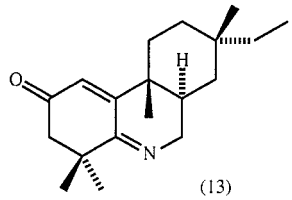
(5) R = COOH
(20) R = $CONH_2$
(25) R = CON_3
(26) R = NCO



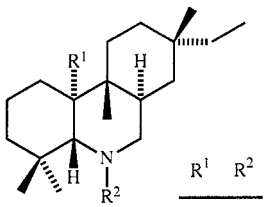
(6) R = COOH
(21) R = $CONH_2$



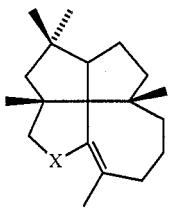
(12)



(13)



	R^1	R^2
(14)	OH	H
(15)	H	H
(16)	H	Ac



(22) X = NH
(24) X = CH_2

* For clarity in the discussion, compounds (11), (12) and (13) have been numbered as diterpenes. Systematic names are quoted in the Experimental section.

[4] Radhakrishna, A. S., Rao, C. G., Varma, R. K., Singh, B. B., and Bhatnagar, S. P., *Synthesis*, 1983, 538.

Hydroxy Imine (11)

The highly crystalline (11) was the predominant product. Its high-resolution mass spectrum supported a molecular formula of $C_{19}H_{33}NO$, while its i.r. spectrum showed hydroxyl absorption at 3370, 3160 and 1123 cm^{-1}, and a peak for the imino function at 1640 cm^{-1}. The ^{13}C n.m.r. spectrum featured one sp^2 carbon signal at δ 175·49 as required for the imino function, in addition to a methylene carbon signal at δ 53·67 as expected for the other nitrogen-bearing carbon. A quaternary carbon peak at δ 73·32 showed that the alcohol function was tertiary. The remaining carbon signals were consistent with a tricyclic system with no further unsaturation.

The ^1H n.m.r. spectrum of (11) showed the conventional methyl signals of the rimuane system as well as signals for the two protons of the nitrogen-substituted methylene group (δ 3·18, J 18·0, 12·0 Hz, and 3·53, J 18·0, 5·2 Hz). The COSY spectrum showed connectivity of these signals to a methine proton resonance (H 8). A broad, one-proton resonance at δ 4·77 ($W_{h/2}$ 16 Hz) which disappeared upon addition of deuterium oxide was also present. These spectral data were consistent with structure (11). The principal fragment from mass spectral breakdown of (11) had *m/z* 153 as would be expected from a retro-Diels–Alder fragmentation of ring B. The other fragment from this cleavage (*m/z* 138) was also apparent.

The hydroxy group was expected to have the α-orientation on mechanistic grounds. This is supported by ^{13}C n.m.r. evidence. The sole methine carbon signal in the spectrum of (11) appeared at δ 28·43. In the spectrum of the subsequently prepared imine (7) which has no hydroxy group, this signal appears at 35·64. A shielding of this magnitude is only to be expected if the C 10 hydroxy group and the C 8 hydrogen bear a 1,3-diaxial relationship. The highest-field methylene carbon signal shows a similar shielding [δ 16·82 in hydroxy imine (11) and 21·15 in imine (7)]. This signal can be assigned to C 2, the only methylene group which is flanked by two other methylene groups. This shielding effect also requires a 10α-hydroxy function.

Lithium aluminium hydride reduction of (11) gave hydroxy amine (14), which was analysed for $C_{19}H_{35}NO$. The i.r. spectrum of (14) showed a broad hydroxyl absorption band at 3354 cm^{-1} and the absence of the C=N absorption band. The ^1H n.m.r. spectrum showed the C 7 proton resonances at δ 2·41 (J 12·1, 12·0 Hz) and 2·96 (J 12·1, 7·5 Hz). The methine proton adjacent to the nitrogen (H 5) produced a doublet at δ 2·48 (J 0·9 Hz). Models show that access to C 5 in (11) would be favoured from the β-face and comparison of the ^1H n.m.r. spectral data with those of the amine (15) (see later) supports this assertion. In particular, the chemical shifts of the respective C 5 protons are very similar which suggests that H 5 and the C 10 hydroxy group are on opposite sides of the ring system in (14). Furthermore, neither the ^1H nor the ^{13}C n.m.r. spectra revealed the temperature dependence which is typical of *cis*-fused systems. The ^{13}C n.m.r. spectrum featured heteronuclear substituted methine (δ 66·85) and methylene (48·63) signals. Comparison of the C 8 methine resonances in (14) and (15) (28·97 and 41·4 respectively), and also the C 2 methylene signal (16·77 and 19·71 respectively) gives further support to the proposed hydroxy group stereochemistry.

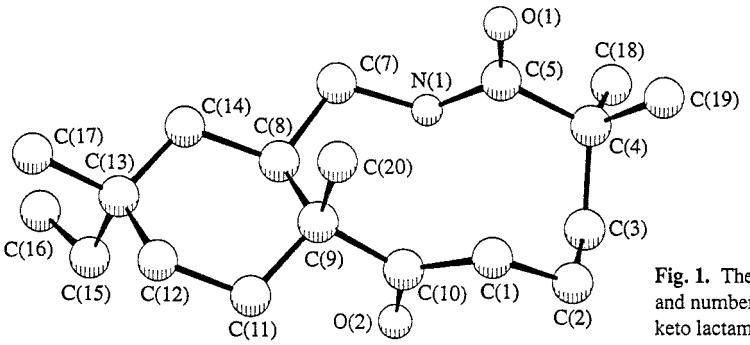


Fig. 1. The molecular structure and numbering scheme for keto lactam (12).

Table 1. Bond lengths (Å) and angles (degrees) for keto lactam (12)

The numbering scheme is given in Fig. 1

Atoms	Bond length	Atoms	Bond angle
N(1)–C(5)	1·34(1)	C(5)–N(1)–C(7)	124·4(9)
N(1)–C(7)	1·45(1)	C(2)–C(1)–C(10)	113·7(8)
C(1)–C(2)	1·52(1)	C(1)–C(2)–C(3)	116·7(7)
C(1)–C(10)	1·51(1)	C(2)–C(3)–C(4)	116·4(8)
C(2)–C(3)	1·54(1)	C(3)–C(4)–C(5)	113·3(8)
C(3)–C(4)	1·53(1)	C(3)–C(4)–C(18)	109·2(8)
C(4)–C(5)	1·57(1)	C(3)–C(4)–C(19)	111·4(7)
C(4)–C(18)	1·54(1)	C(5)–C(4)–C(18)	106·4(7)
C(4)–C(19)	1·52(1)	C(5)–C(4)–C(19)	107·2(8)
C(5)–O(1)	1·19(1)	C(18)–C(4)–C(19)	109·2(8)
C(7)–C(8)	1·50(1)	N(1)–C(5)–C(4)	115·0(9)
C(8)–C(9)	1·57(1)	N(1)–C(5)–O(1)	123(1)
C(8)–C(14)	1·54(1)	C(4)–C(5)–O(1)	122·0(9)
C(9)–C(10)	1·55(1)	N(1)–C(7)–C(8)	113·7(8)
C(9)–C(11)	1·51(1)	C(7)–C(8)–C(9)	117·1(8)
C(9)–C(20)	1·53(1)	C(7)–C(8)–C(14)	110·0(8)
C(10)–O(2)	1·21(1)	C(9)–C(8)–C(14)	110·7(8)
C(11)–C(12)	1·53(1)	C(8)–C(9)–C(10)	107·4(7)
C(12)–C(13)	1·56(1)	C(8)–C(9)–C(11)	108·8(8)
C(13)–C(14)	1·48(1)	C(8)–C(9)–C(20)	109·4(8)
C(13)–C(15)	1·55(2)	C(10)–C(9)–C(11)	107·4(8)
C(13)–C(17)	1·56(1)	C(10)–C(9)–C(20)	112·0(8)
C(15)–C(16)	1·54(1)	C(11)–C(9)–C(20)	111·7(8)
		C(1)–C(10)–C(9)	120·7(8)
		C(1)–C(10)–O(2)	121·5(8)
		C(9)–C(10)–O(2)	117·5(8)
		C(9)–C(11)–C(12)	114·3(8)
		C(11)–C(12)–C(13)	112·9(8)
		C(12)–C(13)–C(14)	109·8(8)
		C(12)–C(13)–C(15)	107·5(9)
		C(12)–C(13)–C(17)	106·0(8)
		C(14)–C(13)–C(15)	113·2(9)
		C(14)–C(13)–C(17)	112·7(9)
		C(15)–C(13)–C(17)	107·3(9)
		C(8)–C(14)–C(13)	116·9(9)
		C(13)–C(15)–C(16)	117(1)

Keto Lactam (12)

The structure of this highly crystalline compound, which analysed for $C_{19}H_{33}NO_2$, was determined by X-ray analysis.

A perspective view of keto lactam (12) is given in Fig. 1. The cyclohexane ring adopts a somewhat flattened chair with most bond angles (Table 1) greater than the tetrahedral value. The cyclohexane ring is *trans* fused to the ten-membered lactam ring. The bond angles (Table 1) at the sp^3 carbon atoms in the lactam ring (mean value 114·0°) are in excess of the tetrahedral value. Bond angles in large rings generally are larger than tetrahedral.[5]

The conformation adopted by the lactam ring could be regarded as deriving from the *trans* fusion [at N(1) and C(1)] of two distorted six-membered rings. The ring defined by atoms N(1),C(7)–C(10),C(1) adopts a distorted chair while the ring defined by atoms N(1),C(1)–C(5) adopts a distorted boat conformation, with N(1) and C(3) involved in the stem–stern interactions. This chair–boat arrangement eliminates the interaction between the methyl C(18) and the carbonyl O(2) which potentially could occur in the chair–chair arrangement.

Ten-membered lactam rings are expected to be flexible, for example, pelargolactam was found to exist as a disordered structure as a result of different ring conformations being present in the solid state.[6] That lactam (12) is conformationally stable at least in the solid state is due in part to weak intermolecular hydrogen bonding between the amide hydrogen and the carbonyl group of the lactam. Respective molecules are linked by hydrogen bonds which extend along the screw axis [O(1)···N(1) (2–x, 1/2+y, 1–z) 3·13(1) Å; ∠O(1)···H–N(1) 165(1)°]. The presence of another carbonyl group C(10) in the lactam ring provides additional rigidity. The carbonyl groups point in opposite directions but are virtually parallel to each other. The angle between the normals to the planes defined by O(1),C(5),N(1) and O(2),C(10),C(1) is 9(1)°. The shortest intermolecular contacts (not involving hydrogen bonding) are between O(1) and O(2), O(1) and C(3) and between O(2) and C(19), at 3·47(1), 3·56(1) and 3·56(1) Å, respectively. These intermolecular contacts will prevent the close approach of adjacent molecules, thereby weakening their hydrogen-bonding interactions.

The ^1H and ^{13}C n.m.r. spectra of (12) showed two distinct sets of signals at room temperature, consistent with the presence of approximately equal concentrations of both (*E*) and (*Z*) configurations of the amide subunit. Variable-temperature ^{13}C n.m.r. studies over the temperature range from −10° to 55° showed a complex pattern of line broadenings and coalescences which suggested that conformational mobility of the ten-membered ring was also playing a part.

Keto Imine (13)

Keto imine (13) was isolated as a minor product. High-resolution mass spectrometry showed a parent ion of *m/z* 287 corresponding to a molecular formula of $C_{19}H_{29}NO$. Absorption bands for a conjugated ketone (1674 cm^{-1}) and a trisubstituted double bond (1601 and 775 cm^{-1}) could be seen in the

[5] Ermer, O., Dunitz, J. D., and Bernal, I., *Acta Crystallogr., Sect. B.*, 1973, **29**, 2278.
[6] Winkler, F. K., and Dunitz, J. D., *Acta Crystallogr., Sect. B.*, 1975, **31**, 281.

i.r. spectrum. The ^{1}H n.m.r. spectrum featured a one-proton singlet at δ 5·96, typical of a conjugated, trisubstituted alkene. An AB pattern (2·38, 2·52, J_{AB} 16·2 Hz) suggested an isolated methylene system adjacent to the keto group (C3). The presence of the nitrogen function connected to C7 as in structures (11) and (12) could be inferred from the two one-proton signals at δ 3·21 (J 9·7, 19·2 Hz) and 3·80 (J 9·7, 4·8 Hz) which showed connectivity in the COSY spectrum to a methine proton signal (H8) at 1·99. The ^{13}C n.m.r. spectrum featured unsaturated carbon signals at δ 199·47, 167·51, 155·69 and 124·12 and showed that (13) was a tricyclic carbonyl compound with a trisubstituted double bond and an imine function. The ultraviolet spectrum revealed an absorption band at 253 nm (ϵ 8682), which indicated that the three unsaturated bonds were conjugated. These features lead to structure (13).

Isolation of the Imine Intermediate (7)

Gas chromatographic analysis during the previously described experiment had shown the presence of an intermediate compound. The structure of the reaction products indicated that this species was likely to be heterocyclic, but its exact nature remained to be determined.

The isolated reaction products were dissolved in ether immediately upon isolation, and this solution was purged with argon. Gas chromatography showed this mixture to contain approximately 60% of the intermediate. Spectra recorded on this product mixture revealed peaks which could be ascribed to the imine (7), in addition to those of compounds (11), (12) and (13). The i.r. spectrum of the mixture showed a strong absorption band at 1644 cm^{-1}, typical of an imine. The ^{13}C n.m.r. spectrum supported an imine structure with an sp^2 carbon signal at δ 177·31. The presence of two methine signals (49·07 and 35·64), and a nitrogen-substituted methylene peak at 52·87 gave further support to the imine structure (7). G.l.c./m.s. showed that the intermediate species gave rise to a parent ion of m/z 275 as required for imine (7).

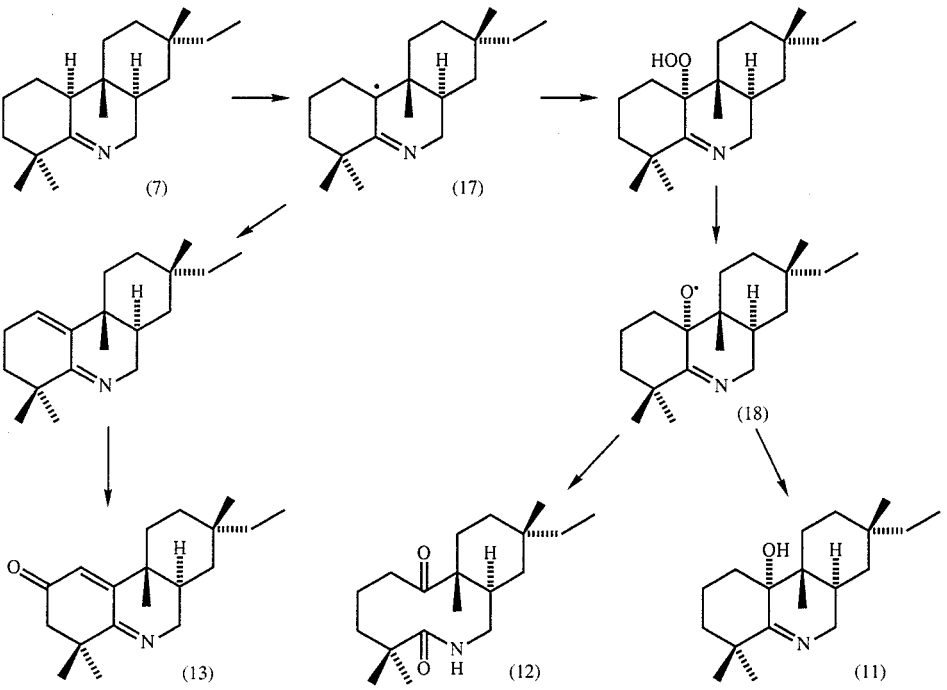
The imino bond of (7) was reduced by treatment with lithium aluminium hydride to give the stable, crystalline amine (15). Microanalysis confirmed the proposed molecular formula. The i.r. spectrum of (15) showed the absence of C=N absorption and the presence of an N–H absorption band at 3470 cm^{-1}. The ^{1}H n.m.r. spectrum showed the C5 proton resonance as a doublet at δ 2·52 with a 5,10-coupling constant of 10·2 Hz. This indicated that the A/B ring junction was *trans*. Thus, hydride addition to the double bond had occurred from the β face as an examination of molecular models would suggest. The proton signals of the nitrogen-substituted methylene (C6) occurred as an ill-defined system centred at 2·50 ppm. The ^{13}C n.m.r. spectrum featured heteronuclear-substituted methine (δ 63·20) and methylene (48·30) carbon signals in support of the proposed structure.

Treatment of amine (15) with acetic anhydride gave the crystalline acetyl derivative (16) which showed a carbonyl absorption at 1651 cm^{-1} and had the expected ^{1}H and ^{13}C n.m.r. spectral characteristics.

Reaction Pathways

The results discussed above show that the treatment of keto amide (8) with iodosylbenzene and formic acid does indeed give the desired imine (7).

However, this imine is extremely sensitive to oxygen and rapidly forms the oxidation products (11), (12) and (13). Formation of these can be reconciled as in Scheme 1, where the key intermediate is the allylic radical (17). Loss of a hydrogen atom from this species can lead, after further allylic oxidation, to the conjugated species (13). Alternatively, formation of the allylic hydroperoxide could give rise to the alkoxy radical (18) which would yield the hydroxy imine (11) by hydrogen atom abstraction or the keto lactam (12) after a β-cleavage process. Production of (12) from the allylic hydroperoxide by an ionic process is also possible.[7]



Scheme 1. Oxidation of imine (7).

The oxidation of imines by molecular oxygen (and by t-butyl hydroperoxide) to form the relatively unstable hydroperoxy imines is a known process.[7,8] These hydroperoxides typically undergo further rearrangement and/or oxidation, and processes involving their intermediacy have been developed for the synthesis of keto lactams similar to (12) (e.g. ref. 6). Keto lactams have also been synthesized by various oxidations of bicyclic enamines,[9–11] and from α-hydroxy imines by peracid oxidation to form oxaziridines which yield keto lactams upon treatment with iron(II) sulfate.[12]

[7] Cohen, L. A., and Witkop, B., *J. Am. Chem. Soc.*, 1955, **77**, 6595.
[8] Schumann, D., Naumann, A., and Wirtz, K. P., *Chem. Ber.*, 1979, **112**, 734.
[9] Mahajan, J. R., Nunes, B. J., Araujo, H. C., and Ferreira, G. A. L., *J. Chem. Res. Miniprint*, 1979, 3158.
[10] Otsuji, Y., Nakanishi, S., Ohmura, N., and Mizuno, K., *Synthesis*, 1983, 390.
[11] Mahajan, J. R., Ferreira, G. A. L., Araujo, H. C., and Nunes, B. J., *Synthesis*, 1976, 112.
[12] Black, D. St.C., and Johnstone, L. M., *Aust. J. Chem.*, 1984, **37**, 599.

Laurenane Derivatives

It was proposed to convert the epimeric keto acids (5) and (6) into the corresponding epimeric imines (2) and (19) by the method described above.

Conversion of the 15β-methyl keto acid (5) into the 15β-methyl keto amide (20) by way of the mixed anhydride proceeded in 90% yield. The crystalline keto amide featured absorption bands in the i.r. spectrum at 3356, 3198, 1682 and 1614 cm^{-1}. The ^1H n.m.r. spectrum contained one-proton multiplets at δ 3·53 ($W_{h/2}$ 25 Hz, H15) and 3·25 (dd, J 11, 7 Hz, H7), a broad two-proton singlet at 2·57 ($W_{h/2}$ 8 Hz, H3), and the amide proton resonances at 6·10 and 5·80. The ^{13}C n.m.r. spectrum showed several broadened signals at 25° reflecting the conformational mobility of the 15β-methyl keto derivatives.[13]

Treatment of (20) with iodosylbenzene/formic acid in aqueous acetonitrile, followed by an aqueous workup, gave imine (2) in 74% yield. This compound analysed for $C_{19}H_{31}N$ and showed the typical imine absorption in the i.r. spectrum (1637 cm^{-1}). That the compound had retained the highly strained laurenane skeleton was supported by the characteristically low-field methyl proton n.m.r. signals (δ 0·89; 1·00; 1·00; 1·17, d, J 6·6 Hz; 1·32) and by the unusually low-field C8 carbon n.m.r. peak (80·30).[14] Other carbon signals and multiplicities were in accordance with the proposed structure. The stereochemistry at C15 was determined by ^1H n.m.r. nuclear Overhauser enhancement difference spectroscopy. Irradiation of H15 (δ 2·68, m, $W_{h/2}$ 24) enhanced the H7 signal (2·46, dd, J 10, 7 Hz) and vice versa. A molecular model showed that this requires the H15 proton to be α and the C15 methyl group to be β. Similar nuclear Overhauser enhancement between H7 and H15 has been observed in lauren-1-ene (1) and in the 15β-methyl keto acid (5).[14]

In a similar manner, the 15α-methyl keto acid (6) was converted into the corresponding keto amide (21) in 70% yield. This compound had i.r. absorbances at 3330, 3200, 1690, 1670 and 1630 cm^{-1}. Its ^1H n.m.r. spectrum had two amide proton signals (δ 5·94, 6·21, both broad) while its ^{13}C n.m.r. spectrum was clearly different from that of its epimer (20), but similar to that of the keto acid (6). Treatment of (21) with iodosylbenzene/formic acid in aqueous acetonitrile, followed by an aqueous workup gave an imine in 64% yield. However, this proved not to be the desired 15α-methyl derivative (19), but rather, the previously isolated 15β-methyl imine (2).

Isomerization of the 15α-methyl imine (19) to the 15-epimer (2) must proceed through their common tautomer, enamine (22). Although the 15α-methyl derivatives are thermodynamically more stable in the 1-keto tricyclic secolaurenanes,[14] the 15β-methyl stereochemistry is favoured in the tetracyclic lauren-1-enes. 15-Epilauren-1-ene (23) has been shown to isomerize to lauren-1-ene (1) under acidic conditions as does the isomeric lauren-1(15)-ene (24).[15] (Note that the 15-epilauren-1-ene used in the isomerization reported in ref. 15 was the major component of a mixture of alkenes and had not been fully characterized. However, 15-epilauren-1-ene has since been produced

[13] Hayman, A. R., Simpson, J., and Weavers, R. T., *Aust. J. Chem.*, 1988, **41**, 1571.
[14] Eaton, P. J., Lauren, D. R., O'Connor, A. W., and Weavers, R. T., *Aust. J. Chem.*, 1981, **34** 1303.
[15] Perry, N. B., and Weavers, R. T., *Aust. J. Chem.*, 1988, **41**, 81.

during a total synthesis of lauren-1-ene.[16] ^1H and ^{13}C spectral data for the samples from the two sources match.)

The yield of 15β-methyl imine (2) from either keto acid (5) or (6) was increased by subjecting the appropriate mixed anhydride derivative to a Curtius degradation. Treatment of the acid anhydride generated from the 15β-methyl keto acid (5) with an aqueous solution of sodium azide gave the 15β-methyl keto azide (25) (characteristic i.r. absorption at 2137 cm^{-1}). Heating (25) under reflux in benzene for two hours effected rearrangement to 15β-methyl keto isocyanate (26) (i.r. peak at 2270 cm^{-1}). Treatment of (26) with potassium t-butoxide/t-butyl alcohol at 30°, followed by a buffered aqueous workup (pH 7·3), gave 15β-methyl imine (2) in 81% overall yield. Repetition of the reaction employing a non-aqueous workup also gave (2), but in reduced yield. When the 15α-methyl keto acid was used as the starting material, the 15β-methyl imine (2) was obtained in 70% overall yield upon aqueous workup. However, in the absence of an aqueous workup an ill-defined mixture was obtained. This, upon hydrolysis, gave a mixture containing only a trace of (2).

Conclusions

The goal of synthesizing 2-azalauren-1-ene (2) has been achieved but it appears that its epimer (19) is readily isomerized to (2) and to date has resisted isolation.

The analogous rimuene-derived imine (7) has been obtained, albeit in an impure state, but this compound is very prone to autoxidation which yields the hydroxy imine (11), the ten-membered ring keto lactam (12) and the conjugated species (13).

Experimental

General

Preparative-layer chromatograms (p.l.c.) were run with 1·25-mm layers of Merck silica $PF_{254+366}$ coated on glass plates.

Radial chromatography was performed on a Harrison Research 7924T Chromatotron with plates coated with a 2 mm layer of Merck silica gel 60 PF_{254} with calcium sulfate binder.

Gas chromatography/mass spectrometry was performed on a Perkin–Elmer 8420 capillary gas chromatograph (fitted with a 10 m DB-1 column supplied by J&W Scientific) connected to a Perkin–Elmer 800 ion trap detector.

High-resolution mass spectra were recorded by Dr P. T. Holland, Ruakura Agricultural Research Centre, Private Bag, Hamilton, New Zealand.

Low-resolution mass spectra were recorded on a Varian MAT CH-7 mass spectrometer.

Infrared spectra were obtained as films or as KBr discs on a Perkin–Elmer 357 double-beam spectrophotometer or on a Nicolet 5MX Fourier transform spectrophotometer.

Ultraviolet spectra were recorded as rectified spirit solutions on a Shimadzu UV-240 spectrophotometer.

^1H and ^{13}C n.m.r. spectra were recorded on a Varian VXR-300 spectrometer operating at 300 MHz for proton and 75·2 MHz for carbon unless otherwise stated. 90-MHz ^1H n.m.r. and 15-MHz ^{13}C n.m.r. spectra were recorded on Varian EM-390 and Jeol FX-60 spectrometers respectively. Samples were examined as $CDCl_3$ solutions and chemical shifts are reported relative to $SiMe_4$.

Microanalyses were recorded by Professor A. D. Campbell or Dr R. G. Cunninghame and associates of our Department.

[16] Crimmins, M. T., and Gould, L. D., *J. Am. Chem. Soc.*, 1987, **109**, 6199.

Keto Amide (8)

A solution of ethyl chloroformate (0·04 ml) in dry tetrahydrofuran (2 ml) was added dropwise to a stirred solution of keto acid (3)[2] (0·160 g) and triethylamine (0·07 ml) in dry tetrahydrofuran (5 ml) at −5°. Stirring was continued for a further 60 min. Aqueous ammonia (0·890, 5 ml) was added dropwise with cooling and stirring was continued for 2 h. The reaction mixture was poured into water (60 ml) and extracted with ether (3×40 ml). The combined ethereal portions were dried over anhydrous magnesium sulfate and evaporated to give *(1″S,1′R,2′S,4′S)-2-(4′-ethyl-1′,3″,3″,4′-tetramethyl-2″-oxoperhydrobiphenyl-2′-yl) acetamide* (8) (0·128 g) (distilled 90°/0·04 mm) (Found: C, 74·9; H, 11·2; N, 4·0. $C_{20}H_{35}NO_2$ requires C 74·7; H, 11·0; N, 4·4%). I.r. ν_{max} 3344, 3165, 1699, 1668, 1615 cm^{-1}. ^1H n.m.r. δ 0·76, t, J 7·5 Hz, 3H; 0·79, s, 3H; 0·96, s, 3H; 1·00, s, 3H; 1·16, s, 3H; 2·80, dd, J 14, 6 Hz, 1H; 5·82, s, $W_{h/2}$ 12 Hz, 1H; 6·18, s, $W_{h/2}$ 12 Hz, 1H. Mass spectrum m/z 321 (M).

Attempted Formation of Imine (7)

A solution of keto amide (8) (0·480 g) in aqueous acetonitrile (25%, 5 ml) was added to a stirred solution of iodosylbenzene (0·360 g) and formic acid (88%, 0·300 g). Stirring was continued for 16 h at room temperature. The reaction mixture was diluted with water (100 ml), acidified with concentrated hydrochloric acid, and ether-extracted (3×50 ml) to remove iodobenzene. The aqueous layer was basified with sodium hydroxide (10%) and extracted with ether (3×50 ml) to give a white crystalline product (0·405 g). Radial chromatography (ether/hexane 6 : 4) gave the following compounds in order of elution.

(i) *(6aR,8S,10aR,10bS)-8-Ethyl-4,4,8,10a-tetramethyl-1,2,3,4,6,6a,7,8,9,10,10a,10b-dodecahydrophenanthridin-10b-ol* (11) (0·190 g). I.r. ν_{max} 3360, 3160, 1638, 1123, 970 cm^{-1}. ^1H n.m.r. (360 MHz) δ 0·74, s, 3H; 0·76, t, J 6·5 Hz, 3H; 0·82, s, 3H; 1·11, s, 3H; 1·28, s, 3H; 1·98, m, $W_{h/2}$ 25 Hz, 1H; 3·08, dd, J 18·0, 12·0 Hz, 1H; 3·52, dd, J 18·0, 5·2 Hz. ^{13}C n.m.r. (90·5 MHz) δ 7·96, q; 15·11, q; 16·82, t; 25·19, t; 28·09, t; 28·43, d; 28·94, q; 29·67, q; 29·98, q; 30·93, t; 32·36, s; 32·64, t; 36·28, t; 37·46, s; 39·61, s; 40·03, t; 53·67, t; 73·32, s; 175·49, s. Mass spectrum m/z 291·2562 (M) ($C_{19}H_{33}NO$ requires 291·2562), 274, 153, 138.

(ii) *(6aR,8S,10aR)-8-Ethyl-4,4,8,10a-tetramethyl-3,4,6a,7,8,9,10,10a-octahydrophenanthridin-2(6H)-one* (13) (0·040 g) λ_{max} 253 (ϵ 8682) nm. I.r. ν_{max} 1674, 1601, 775 cm^{-1}. ^1H n.m.r. (90 MHz) δ 0·73, t, J 7·5 Hz, 3H; 0·84, s, 3H; 0·87, s, 3H; 1·14, s, 3H; 1·21, s, 3H; 1·99, m, $W_{h/2}$ 18 Hz, 1H; 2·38, d, J 16·2 Hz, 1H; 2·52, d, J 16·2 Hz, 1H; 3·21, dd, J 9·7, 19·2 Hz, 1H; 3·80, dd, J 9·7, 4·8 Hz, 1H; 5·96, s, 1H. ^{13}C n.m.r. (15·04 MHz) δ 7·88, q; 15·95, q; 26·96, q; 27·19, q; 28·03, t; 28·82, q; 30·43, t; 32·45, s; 32·68, t; 34·93, d; 35·14, s; 35·97, t; 41·90, s; 51·77, t; 54·20, t; 124·12, d; 155·69, s; 167·61, s; 199·47, s. Mass spectrum m/z 287·2249 (M) ($C_{19}H_{29}NO$ requires 287·2249).

(iii) *(8aR,11S,12aR)-11-Ethyl-4,4,8a,11-tetramethylperhydro-2-benzazecine-3,8-dione* (12) (0·120 g) distilled 96°/0·03 mm) (Found: C, 74·3; H, 11·0; N, 4·5. $C_{19}H_{33}NO_2$ requires C, 74·2; H, 10·8; N, 4·6%). I.r. ν_{max} (CCl_4) 3464, 1690, 1667 cm^{-1}. ^1H n.m.r. δ 0·78, t, J 6·9 Hz, 3H; 0·82, t, J 6·9 Hz, 3H; 0·83, s, 3H; 0·85, s, 3H; 1·04, s, 3H; 1·08, s, 6H; 1·12, s, 6H; 1·20, s, 3H; 5·32, m, $W_{h/2}$ 26 Hz, 1H; 5·67, s, $W_{h/2}$ 22 Hz, 1H. ^{13}C n.m.r. δ 7·83, q; 7·90, q; 12·76, q; 13·68, q; 18·20, t; 18·30, t; 23·40*, q; 24·53*, q; 26·40*, q; 27·98*, q; 28·06, t; 28·42, t; 28·55*, t; 28·71, q; 28·79, q; 31·48, t; 31·79, t; 31·79, t; 31·79, t; 32·76, s; 32·82, s; 35·09, t; 35·17, d; 36·40, t; 36·62, t; 37·31*, t; 38·85, t; 40·77, s; 40·92, s; 41·76, t; 42·84, t; 43·15, d; 49·70, s; 51·39, s; 176·76, s; 178·20, s; 216·64, s; 219·64, s. Peaks marked with * were broadened at 25°. Mass spectrum m/z 307 (M).

X-Ray Structure Determination of Keto Lactam (12)

Keto lactam (12) crystallized as rhombs from an ether/hexane mixture, and a single crystal with dimensions 0·44 by 0·23 by 0·14 mm was used for X-ray measurements.

Crystal data.—$C_{19}H_{33}NO_2$, M 307·46, monoclinic, space group $P2_1$, a 7·168(2), b 9·962(3), c 12·579(3) Å, β 103·64(2)°, U 872·9(4) $Å^3$, D_m (flotation) 1·13(2), D_c 1·17 g cm^{-3}, Z 2, F(000) 340, λ 0·7107 Å, μ(Mo Kα) 0·41 cm^{-1}, T 123 K.

Preliminary oscillation and Weissenberg photography indicated the monoclinic system (systematic absences implied $P2_1$ or $P2_1/m$). A total of 2059 independent intensities were measured on a Nicolet P3 fully automatic four-circle diffractometer in conventional θ–2θ scan mode ($2\theta_{max}$ 45°). Three standard reflections monitored every 100 reflections indicated negligible crystal instability. Lorentz and polarization corrections were applied, but no correction was made for absorption. The data were averaged to give 1063 unique observed intensities [$I > 2 \cdot 5\sigma(I)$]. Cell dimensions were derived from the angular measurement of 25 strong reflections in the range $29 < 2\theta < 30°$.

Table 2. Atomic coordinates and equivalent or isotropic thermal parameters for keto lactam (12)

The numbering scheme is given in Fig. 1. Equivalent isotropic U (Å^2) defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	X/a	Y/b	Z/c	U_{eq}/U_{11}
C(1)	0·518(1)	0·872(1)	0·4701(7)	0·022(2)
C(2)	0·583(1)	0·812(1)	0·5839(7)	0·024(2)
C(3)	0·802(1)	0·797(1)	0·6294(7)	0·019(2)
C(4)	0·921(1)	0·925(1)	0·6346(7)	0·018(2)
C(5)	0·923(1)	0·983(1)	0·5189(8)	0·021(2)
C(7)	0·946(1)	0·922(1)	0·3321(7)	0·021(2)
C(8)	0·791(1)	0·846(1)	0·2533(7)	0·020(2)
C(9)	0·581(1)	0·857(1)	0·2703(7)	0·020(2)
C(10)	0·582(1)	0·792(1)	0·3828(7)	0·014(2)
C(11)	0·449(1)	0·774(1)	0·1838(7)	0·025(3)
C(12)	0·455(1)	0·811(1)	0·0662(7)	0·025(2)
C(13)	0·663(1)	0·807(1)	0·0468(8)	0·025(2)
C(14)	0·795(1)	0·881(1)	0·1347(7)	0·028
C(15)	0·719(2)	0·657(1)	0·0402(8)	0·030
C(16)	0·910(2)	0·627(2)	0·010(1)	0·051
C(17)	0·647(2)	0·870(2)	−0·0685(8)	0·038
C(18)	1·132(1)	0·894(1)	0·6915(8)	0·028
C(19)	0·847(2)	1·035(1)	0·6975(8)	0·025
C(20)	0·520(2)	1·005(1)	0·2651(8)	0·026
O(1)	0·899(1)	1·100(1)	0·4982(5)	0·028
O(2)	0·620(1)	0·674(0)	0·3944(5)	0·024
N(1)	0·954(1)	0·893(1)	0·4462(6)	0·017

Structure determination.—The structure was solved by direct methods with MULTAN.[17] The six-membered ring and part of the ten-membered lactam ring were located in the first ranked figure-of-merit solution produced by the program. Subsequent difference syntheses using SHELX76[18] revealed the sites of all remaining non-hydrogen atoms. The structure of the enantiomorph based on the stereochemistry of (+)-rimuene[19] was refined by full-matrix least-squares. Hydrogen atoms were included in calculated positions (C–H = 1·08 Å) with fixed isotropic temperature factors. The methyl and ethyl carbons and the nitrogen and oxygen atoms were assigned anisotropic thermal parameters. Complex neutral atom scattering factors[20] were employed, with weighting scheme $w = 2 \cdot 2821/[\sigma^2(F_0) + 0 \cdot 00056\ |F_0^2|]$. The

[17] Main, P., Lessinger, L., and Woolfson, M. M., 'MULTAN 77' Department of Physics, University of York, England, 1977.

[18] Sheldrick, G. M., 'SHELX76 Program for Crystal Structure Determination', University of Cambridge, England, 1976.

[19] Klyne, W., and Buckingham, J., 'Atlas of Stereochemisty' 2nd Edn, Vol. 1, p. 108 (Chapman and Hall: London 1978).

[20] Ibers, J. A., and Hamilton, W. C., (Eds) 'International Tables for X-Ray Crystallography' Vol. 4 (Kynoch Press: Birmingham 1974).

final conventional $R = 0.0880$ and $R_w = 0.0812$. The high R values reflect the poor quality of the crystal used for data collection; no better crystals could be obtained. The final difference map showed no peaks greater than 0·43 e Å^{-3} in height. Bond lengths and angles are given in Table 1 and final atomic coordinates in Table 2. Material deposited: anisotropic thermal parameters, hydrogen atom coordinates, and lists of structure factors.*

Hydroxy Amine (14)

A solution of hydroxy imine (11) (0·120 g) in dry ether (20 ml) was heated under reflux with excess of lithium aluminium hydride for 2 h. The reaction mixture was cooled and treated with excess of sodium sulfate decahydrate. Filtration and evaporation gave *(4aR,6aR,8S,10aR,10bR)-8-ethyl-4,4,8,10a-tetramethylperhydrophenanthridin-10b-ol* (14) (0·112 g) (distilled 86°/0.03 mm) (Found: C, 77·6; H, 11·8; N, 4·6. $C_{19}H_{35}NO$ requires C, 77·8; H, 12·0; N, 4·8%). I.r. ν_{max} 3354 cm^{-1}. ^{1}H n.m.r. δ 0·80, t, J 7·2 Hz, 3H; 0·86, s, 3H; 0·94, s, 3H; 1·06, s, 3H; 1·15, s, 3H; 2·41, dd, J 12·1, 12·0 Hz, 1H; 2·48, d, J 0·9 Hz, 1H; 2·96, dd, J 12·1, 7·5 Hz, 1H. ^{13}C n.m.r. δ 7·93, q; 16·77, t; 17·09, q; 25·73, q; 27·14, t; 27·29, t; 28·08, t; 28·46, q; 28·97, d; 31·09, q; 32·33, t; 32·48, s; 33·14, s; 34·53, t; 38·09, t; 39·95, s; 48·63, t; 68·85, d; 76·23, s. Mass spectrum m/z 293 (M), 277, 139.

Identification of Imine (7)

Reaction of keto amide (8) (0·296 g) with iodosylbenzene/formic acid as previously described, gave a crystalline product (0·202 g), which was immediately dissolved in dry ether and the solution saturated with argon. G.l.c./m.s. of this solution showed peaks due to hydroxy imine (11) (relative retention time 1·24), conjugated imine (13) (relative retention time 1·33) and keto lactam (12) (relative retention time 1·52) as well as the peak ascribed to imine (7) (relative retention time 1·00) which comprised approximately 60% of the mixture. Spectra of this mixture showed peaks additional to those of compounds (11), (12) and (13), which were consistent with structure (7). I.r. ν_{max} 1644 cm^{-1}. ^{1}H n.m.r. δ 0·74, s, 3H; 0·82, t, J 7·5 Hz, 3H; 0·88, s, 3H; 1·13, s, 3H; 1·17, s, 3H. ^{13}C n.m.r. δ 7·91, q; 13·61, q; 21·15, t; 25·88, t; 28·17, t; 28·37, 2×q; 29·04, q; 32·39, t; 32·60, t; 33·35, s; 35·64, d; 35·84, t; 36·29, 2×s; 40·27, t; 49·07, d; 52·97, t; 177·31, s. Mass spectrum m/z 275 (M).

Amine (15)

A solution of the mixture containing imine (7) (0·100 g) in dry ether was heated under reflux with excess of lithium aluminium hydride for 2 h. The reaction mixture was cooled and treated with excess of sodium sulfate decahydrate. Filtration and evaporation gave an oil (0·096 g). Column chromatography (alumina), and elution with ether/hexane 6 : 4 gave *(4aS,6aR,8S,10aR,10bS)-8-ethyl-4,4,8,10a-tetramethylperhydrophenanthridine* (15) (0·050 g) (distilled 90°/0·03 mm) (Found: C, 82·2; H, 12·9; N, 4·80. $C_{19}H_{35}N$ requires C, 82·2; H, 12·7; N, 5·1%). I.r. ν_{max} 3470 cm^{-1}. ^{1}H n.m.r. δ 0·76, t, J 7·5 Hz, 3H; 0·80, s, 6H; 0·90, s, 3H; 0·95, s, 3H; 1·78, m, $W_{h/2}$ 18 Hz, 1H; 2·50, d, J 10·2 Hz, 1H; 2·44–2·57, m, 2H. ^{13}C n.m.r. δ 8·13, q; 11·87, q; 19·71, t; 21·87, t; 24·80, q; 28·69, t; 29·22, q; 30·22, q; 32·72, s; 32·99, t; 34·30, t; 34·36, s; 35·45, s; 36·02, t; 41·21, d; 41·67, t; 48·11, d; 48·30, t; 63·20, d. Mass spectrum m/z 277 (M), 206.

Amine Acetate (16)

A solution of amine (15) (0·068 g) in acetic anhydride (5 ml) was heated under reflux for 10 min. The reaction mixture was diluted with water (50 ml), basified with sodium hydroxide (10%) and extracted with ether (4×40 ml). The combined ethereal portions were dried over anhydrous magnesium sulfate and evaporated. Column chromatography (alumina), and elution with ether gave *(4aS,6aR,8S,10aR,10bS)-8-ethyl-4,4,8,10a-tetramethylperhydrophenanthridin-5-yl ethanone* (16) (0·060 g). I.r. ν_{max} 1651 cm^{-1}. ^{1}H n.m.r. δ 0·72, s, 3H; 0·83, t, J 7·5 Hz, 3H; 0·90, s, 3H; 0·98, s, 3H; 1·03, s, 3H; 2·17, s, 3H; 3·22, m, $W_{h/2}$ 32 Hz, 1H;

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3·63, m, $W_{h/2}$ 30 Hz, 1H; 4·03, m, $W_{h/2}$ 28 Hz. ^{13}C n.m.r. δ 8·31, q; 12·08, q; 21·61, q; 23·21, t; 23·39, q; 26·69, t; 29·00, t; 29·18, q; 29·85, s; 30·50, q; 33·05, t; 33·60, s; 34·45, t; 38·93, t+s; 40·89, t; 41·04, d; 47·14, d; 48·70*, t; 61·80*, d; 171·93, s (peaks labelled * were markedly broadened). Mass spectrum *m/z* 319·2869 (M) ($C_{21}H_{37}NO$ requires 319·2875), 304, 248, 206.

15β-Methyl Keto Amide (20)

Amination of the mixed anhydride of 15β-keto acid (5)[3] (0·320 g) by the method described above for the conversion of (3) into (8), gave *1-oxo-1,2-secolaurenan-2-amide* (20) (0·285 g) (distilled 96°/0·03 mm) (Found: C, 75·0; H, 10·7; N, 4·2. $C_{20}H_{33}NO_2$ requires C, 75·2; H, 10·4; N, 4·4%). I.r. ν_{max} 3356, 3198, 1682, 1614 cm^{-1}. ^{1}H n.m.r. δ 1·01, d, *J* 6·3 Hz, 3H; 1·11, s, 3H; 1·14, s, 3H; 1·24, s, 3H; 1·44, s, 3H; 2·57, s, $W_{h/2}$ 8 Hz, 2H; 3·25, dd, *J* 11, 7 Hz, 1H; 3·53, m, $W_{h/2}$ 24 Hz, 1H, 5·80, s, $W_{h/2}$ 15 Hz, 1H; 6·10, s, $W_{h/2}$ 15 Hz, 1H. ^{13}C n.m.r. δ 17·29, q; 22·18*, t; 23·81*, q; 26·46*, q; 26·82, t; 28·85, q; 35·22, q; 35·22*, t; 37·83, s; 39·95*, d; 42·87, t; 46·75, t; 47·45*, t; 48·59, s; 49·77, s; 57·84, t; 58·64, d; 79·77, s; 176·43, s; 218·36, s (peaks labelled * were markedly broadened). Mass spectrum *m/z* 319 (M).

Imine (2)

Treatment of 15β-methyl keto amide (20) (0·120 g) with iodosylbenzene/formic acid as described for the attempted formation of imine (7) from keto amide (8), gave the crystalline *2-azalauren-1-ene* (2) (0·076 g) (sublimed 100°/0·02 mm) (Found: C, 83·3; H, 11·3; N, 5·0. $C_{19}H_{31}N$ requires C, 83·5; H, 11·4; N, 5·1%). I.r. ν_{max} 1637 cm^{-1}. ^{1}H n.m.r. δ 0·89, s, 3H; 1·00, s, 3H; 1·04, s, 3H; 1·17, d, *J* 6·6 Hz, 3H; 1·32, s, 3H; 1·56, s, 2H; 2·46, dd, *J* 10, 7 Hz, 1H; 2·68, m, $W_{h/2}$, 1H; 3·35, d, *J* 15·6 Hz, 1H; 3·64, d, *J* 15·6 Hz, 1H. ^{13}C n.m.r. δ 20·32, q; 20·82, t; 22·60, q; 24·92, t+q; 28·14, q; 32·48, d; 33·42, q; 33·97, t; 38·87, s; 40·39, t; 41·44, t; 48·25, s; 53·68, s; 59·40, d; 60·11, t; 72·98, t; 80·30, s; 188·38, s. Mass spectrum *m/z* 273 (M).

15α-Methyl Keto Amide (21)

Amination of the mixed anhydride of 15α-keto acid (6)[3] (0·160 g) by the method described above for the conversion of (3) into (8), gave *1-oxo-1,2-seco-15βH-laurenan-2-amide* (21) (0·111 g) (sublimed 170°/0·01 mm) (Found: C, 75·5; H, 10·3; N, 4·2. $C_{20}H_{33}NO_2$ requires C, 75·2; H, 10·4; N, 4·4%). I.r. ν_{max} 3330, 3200, 1690, 1670, 1630 cm^{-1}. ^{1}H n.m.r. (90 MHz) δ 1·07, d, *J* 6 Hz, 3H; 1·11, s, 3H; 1·28, s, 3H; 1·47, s, 3H; 1·50, s, 3H; 5·94, br s, 1H; 6·21, br s, 1H. ^{13}C n.m.r. (15·04 MHz) δ 18·43, q; 21·52, q; 21·85, t; 23·47, t; 24·85, q; 29·08, q; 32·89, q; 38·01, t; 38·25, s; 44·26, t; 45·08, s; 46·38, t+d; 47·67, t; 48·73, s; 56·45, t+d; 82·19, s; 174·13, s; 219·94, s. Mass spectrum *m/z* 319 (M).

Attempted Synthesis of Imine (19)

Treatment of the 15α-methyl keto amide (21) (0·080 g) with iodosylbenzene/formic acid as described for the attempted formation of imine (7) from keto amide (8), gave 2-azalauren-1-ene (2) (0·44 g), identical (^{1}H and ^{13}C n.m.r. and g.l.c.) with the sample prepared from the 15β-methyl keto amide (20). 15α-Methyl keto amide (21) (0·024 g) was recovered from the neutral extract.

Imine (2) by Curtius Degradation

(a) From 15β-methyl keto amide (20).—A solution of ethyl chloroformate (0·04 ml) in dry tetrahydrofuran (2 ml) was added dropwise to a stirred solution of keto acid (5) (0·160 g) and triethylamine (0·07 ml) in dry tetrahydrofuran (5 ml) at −5°. Stirring was continued for a further 60 min. Aqueous sodium azide (10%, 5 ml) was added and stirring was continued for 15 min at 0° and for a further 15 min at room temperature. The reaction mixture was diluted with water (50 ml) and extracted with ether (3×40 ml). The combined ethereal portions were

dried over anhydrous magnesium sulfate and evaporated to give crude 15β-methyl keto azide (25) (0·135 g) (i.r. ν_{max} 2137 cm^{-1}).

A solution of the azide in benzene was heated under reflux for 2 h. Evaporation of the solvent gave crude 15β-methyl keto isocyanate (26) (0·130 mg) (i.r. ν_{max} 2270, 1732 cm^{-1}).

A solution of the isocyanate in dry t-butyl alcohol (10 ml) was treated with potassium t-butoxide (0·080 g) at 30° for 30 min. The reaction mixture was poured into an aqueous phosphate buffer (pH 7·3, 60 ml) and extracted with ether (4×40 ml). The combined ethereal portions were dried over anhydrous magnesium sulfate and evaporated to give 2-azalauren-1-ene (2) (0·057 g).

(b) From 15α-methyl keto amide (21).—Repetition of the above procedure by using the 15α-methyl keto amide (21) (0·110 g), gave 2-azalauren-1-ene (2) (0·057 g).

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