Tetrahedron, 1966, Vol. 22, pp. 1701 to 1708. Pergamon Press Ltd. Printed in Northern Ireland

THE CHEMISTRY OF THE TETRACYCLIC DITERPENOIDS—II

THE SHAPE OF RING B OF THE KAURENOLIDES

J. R. HANSON
The Chemical Laboratory, University of Sussex, Brighton, Sussex

(*Received* 11 *September* 1965)

Abstract—Ring B of the kaurenolides has been shown to exist in a twisted boat form. Some 7α–20 ethers have been produced by photolytic methods.

THE tetracyclic diterpenoids contain more pendant groups on a perhydrophenanthrene skeleton than the steroids thus increasing the number of diaxial interactions and the consequent possibilities of skeletal distortion from all-chair forms. It is the purpose of this paper to examine one of these deformations and its influence on the reactions of this group of diterpenoids. Part of this work is the subject of a preliminary communication.[1] The reactions of ring B of the kaurene–atisine group of diterpenes reveal the participation of both chair and boat forms. Thus on the one hand the elimination and cleavage reactions of 7-hydroxy kaurenolide (1)[2] are those diagnostic of chair forms whilst on the other hand the ether and internal hydrogen transfer reactions of the alkaloids,[3] imply the participation of boat forms. Therefore to obtain an indication of the ground state conformation of ring B in the kaurenolides we measured the coupling constants between the C(5), C(6) and C(7) protons for a series of 7-epimers. These results are tabulated.

The parameters of the Karplus equation[7] appear to be dependent on the chemical nature of the coupled fragment.[8,9] A set of parameters closely related to those of other workers was found to be satisfactory.

$$J_{AB} = 12{\cdot}4 \cos^2 \phi \qquad 0 < \phi < 90^\circ$$
$$J_{AB} = 14{\cdot}3 \cos^2 \phi \qquad 90 < \phi < 180^\circ$$

Although the application of a simple equation to the calculation of dihedral angles has been the subject of considerable criticism[10] nevertheless the relationship between the coupling constant and dihedral angle would seem to be of this form. Since the coupling constants lie in the steeply changing portion of the curve variations of ±0·5

---

[1] D. H. R. Barton, J. R. Hanson, *Chem. Comm.* 117 (1965).

[2] B. E. Cross, R. H. B. Galt, J. R. Hanson and W. Klyne, *Tetrahedron Letters* 145 (1962).

[3] D. Dvornik and O. E. Edwards, *Tetrahedron* **14,** 54 (1961).

[4] S. W. Pelletier, *Tetrahedron* **14,** 76 (1961); *Experentia* **20,** 1 (1964).

[5] B. E. Cross, R. H. B. Galt and J. R. Hanson, *J. Chem. Soc.* 3783 (1963).

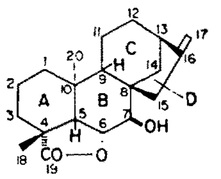
[6] J. R. Hanson, to be published.

[7] M. Karplus, *J. Chem. Phys.* **30,** 11 (1959).

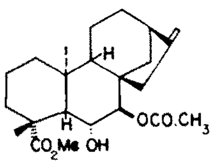
[8] For a recent review see C. N. Banwell and N. Sheppard, *Disc. Farad. Soc.* **30,** 115 (1962).

[9] J. R. U. Lemieux and R. Lown, *Tetrahedron Letters* 1229 (1963); M. Karplus, *J. Amer. Chem. Soc.* **85,** 2870 (1963).

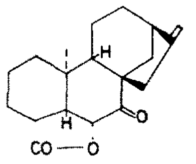
[10] D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.* **86,** 2742 (1964).



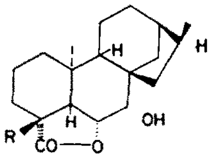
I



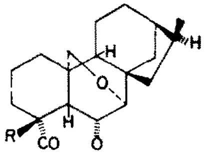
II



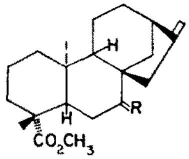
.III



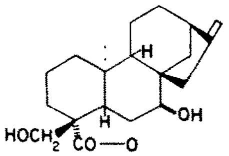
IV a $R = CH_3$
IV b. $R = H$



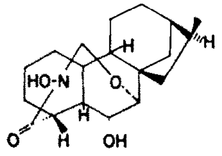
V a $R = CH_3$
V b $R = H$



VI a. $R = O$
VI b $R = {}^{H}_{OH}$



VII



VIII

in the parameters of the Karplus equation introduce variations of only ±3° in the calculated dihedral angles. Furthermore since epimeric pairs of compounds were used in these calculations the results must be mutually consistent. Hence without wishing to specify the exact values of the angles involved, it is possible to distinguish between chair, boat and twisted boat forms. Thus for a chair form $\phi(6\beta{:}7\alpha) + \phi(6\beta{:}7\beta)$ should approximate to 120° whilst for a twisted boat form $\phi(6\beta{:}7\alpha) - \phi(6\beta{:}7\beta)$ should approximate to 120°. The average value of $J_{6\beta:7\alpha}$ of 6·75 corresponds to a dihedral angle of 43° or 146 ± 3° between these protons whilst $J_{6\beta:7\alpha}$ of 7·75 corresponds to an angle of 22° or 137° ± 3°. Of these the values of 140° and 22° are reasonably consistent and hence we conclude that in the kaurenolides, in which the lactone ring is present, ring B exists in a twisted boat form with C(6) at one of the points.[11]

The compounds used in this study were prepared by methods described elsewhere.[2,5,6] Thus reduction of the 7-ketones with sodium borohydride gave the corresponding 7α-alcohols, the reagent attacking from the less hindered face of the molecule.

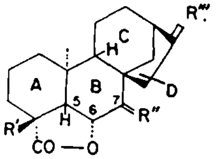
The spectra of a number of 6:7 diols and 7-acylated diols were also examined.

---

[11] C. Djerassi and W. Klyne, *Proc. New York Academy of Sciences* **48**, 1093 (1962).

Table 1. The chemical shifts of the 6 and 7-protons in the kaurenolides

	R′	R″	R‴	τ_6	$J_{5:6}$	τ_7	$J_{6:7}$	Ref.
1.	CH_3	▲OH ╲H	$=CH_2$	5·20	6·5	5·65	6·5	2
2.	CH_3	▲H ╲OH	$=CH_2$	—	—	5·92	7·5	2
3.	CH_2OH	▲OH ╲H	$=CH_2$	5·21	7·0	5·68	7·0	5
4.	CH_2OH	▲H ╲OH	$=CH_2$	—	—	5·95	7·5	6
5.	CH_3	▲OAc ╲H	$=CH_2$	5·21	6·5	4·10	6·5	2
6.	CH_3	▲H ╲OAc	$=CH_2$	—	—	4·70	8·0	2
7.	CH_3	▲OAc ╲H	$=O$	5·35	6·5	4·20	6·5	2
8.	CH_3	▲H ╲OAc	$=O$	5·10	6·0	4·70	8·0	6
9.	CH_2OTs	▲OH ╲H	$=CH_2$	5·25	6·5	5·55	6·5	5
10.	CH_2OTs	▲H ╲OH	$=CH_2$	—	—	5·88	8·0	6
11.	CH_2OTs	▲OTs ╲H	$=CH_2$	5·40	6·5	4·60	6·5	6
12.	CH_3	▲OTs ╲H	$=CH_2$	5·38	6·5	4·57	6·5	2
13.	CH_2OAc	▲OAc ╲H	$=CH_2$	5·30	7·0	4·23	7·0	5
14.	CH_2OAc	▲OAc ╲H	$=O$	5·31	7·0	4·23	7·0	6
15.	CH_3	$=O$	$=CH_2$	5·15	5·5	—	—	2
16.	CH_2OH	$=O$	$=CH_2$	4·95	6·0	—	—	5
17.	CO_2CH_3	$=O$	$=O$	5·21	6·5	—	—	5
18.	H	$=O$	$=CH_2$	5·32	6·5	—	—	5



In most cases the 6- and 7-protons were incompletely resolved and it was impossible to obtain a complete set of coupling constants. However $J_{6\beta:7\beta}$ is approximately 2–3 c/s as in the acetyl derivative (II). This corresponds to an angle of about 60° indicating that in these compounds ring B is nearer to an undistorted chair form thus accommodating the earlier experimental results.

Williamson and Johnson derived[12] an expression of the Karplus equation for some steroidal α-acetoxy ketones. This equation was used for the analogous 7-keto-lactones which showed an average $J_{5:6}$ of 6 c/s corresponding to an angle of 39° ± 3° between these protons and hence to a partially twisted form. In addition to showing a doublet at 5·32 ($J_{5:6} = 6$ c/s) the spectrum of the keto-lactones (III) showed a triplet at 7·35 arising from the 5-proton in which $J_{4:5} = J_{5:6} = 6$ c/s. Hence the lactone ring remained diaxial despite the loss of an equatorial 18-substituent. These results suggest that in the kaurenolides distortion of ring A of the type displayed by the 4,4-dimethyl steroids[13] may be relayed to ring B by the lactone ring.

One consequence of this conformation of ring B is the juxta-position of the angular C-10 methyl and the C-7α-hydroxyl groups. A six-membered transition state has been proposed for photochemical substitution reactions.[14] However a 7–20 ether has been reported[2] in this series from a thermal reaction with lead tetraacetate and it was therefore of interest to apply photochemical transformations in order to seek exceptions to the rule. Irradiation of the 7α-alcohol (IVa) in the presence of iodine and lead tetraacetate[15] for 3 hr, gave a good yield of an ether, $C_{20}H_{28}O_3$ together with only a trace of the corresponding 7-ketone. Comparison of the NMR spectrum with that of the starting material revealed the loss of the C-10 methyl resonance at $\tau = 9$, and the appearance of a 2-proton methyleneoxy group at 6·42 τ. The C-7 proton remained coupled to the C-6 proton which appeared as a double-doublet at $\tau = 5{\cdot}28$ (J = 3·5 and 7·5 c/s). Further evidence for the structure (Va) was obtained as follows. Although the ether was recovered unchanged after attempted hydrolysis with 1N NaOH, reduction with LAH afforded a diol-ether. This on oxidation with chromium trioxide gave a lactonol in which the C-7 resonance had now collapsed to a singlet. Furthermore reduction of the lactonol with LAH furnished the parent ether (Va) thus removing the possibility of C–C bond fission during the reaction sequence. Since reduction of a 6-ketone has been shown to lead to axial products,[6] this also established the stereochemistry at C-6 which could have been inverted during photolysis.[16] Hence we may conclude that the photochemical ether formation reaction may under these favourable circumstances, utilize a seven-membered transition state.

Reduction of the 7-keto-ester (VIa)[2] with sodium borohydride gave the 7α-alcohol (VIb) which on irradiation with lead tetraacetate and iodine in benzene gave only intractable material.

---

[12] K. Williamson and W. S. Johnson, *J. Amer. Chem. Soc.* **83**, 4623 (1961).

[13] D. H. R. Barton, D. A. Lewis and J. F. McGhie, *J. Chem. Soc.* 2907 (1957); D. H. R. Barton and G. A. Morisson, *Fortschr. Chem. Org. Naturstoffe* **19**, 166 (1961).

[14] cf. M. Akhtar and S. Marsh, *Tetrahedron Letters* 2475 (1964); J. W. ApSimon and O. E. Edwards, *Canad. J. Chem.* **40**, 896 (1962); W. L. Meyer and A. S. Levinson, *Proc. Chem. Soc.* 15 (1963); R. F. C. Brown, *Austral. J. Chem.* **17**, 47, (1964).

[15] C. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner and A. Wettstein, *Experientia* **17**, 475 (1961); *Helv. Chim. Acta* **45**, 1317 (1962).

[16] K. Heusler, J. Kalvoda. G. Anner and A. Wettstein, *Helv. Chim. Acta* **46**, 352 (1963).

Owing to the scarcity of 7-hydroxykaurenolide, photolysis of the nitrite[17] was examined in the 18-nor series. 7,18-Dihydroxykaurenolide (VII) on vigorous oxidation gave, *inter alia*, the keto-lactone (III)[1] which was reduced with sodium borohydride to the 7α-alcohol (IVb). Catalytic hydrogenation followed by careful crystallization led to the isolation of the β-dihydro compound. Alternatively reduction of 7,18-dihydroxykaurenolide over 10% palladised charcoal followed by fractional crystallization gave β-dihydro-7,18-dihydroxykaurenolide, m.p. 223–224°. On treatment with toluene-*p*-sulphonyl chloride in pyridine this formed both a mono and ditoluene-*p*-sulphonate. Reduction of the former with LAH led to a triol. The same triol, 6α,7β,19-trihydroxy-16-epi-(—)-kaurane was obtained by reduction of β-dihydro-7-hydroxykaurenolide thus establishing a relationship between the dihydro series. Oxidation of the kauranolide with the 8N CrO_3 reagent followed by decarboxylation gave the corresponding 18-nor-7-keto-lactone which on reduction with sodium borohydride formed the 7α-alcohol. Reduction of this alcohol with LAH gave a triol. The NMR spectrum of this and the corresponding triol from 7α-hydroxykaurenolide, which was prepared by reduction of methyl 6α,7α-dihydroxy-(—)-kaur-16-en-19-oate, both possess a two proton resonance at $\tau = 6{\cdot}10$ which may be assigned to the axial 19-hydroxymethyl group.[18] Thus in accord with the evidence discussed earlier, epimerization at C(4) has not taken place during the preparation of the 18-nor-lactones.

Irradiation of the 18-nor-7α-hydroxykauranolide in the presence of lead tetra-acetate and iodine gave as expected a 7–20 ether (Vb). Photolysis of the nitrite followed by heating with isopropanol gave a lactam, $C_{19}H_{27}O_4N$ ν_{max} 1640^{-1}. Comparison of the NMR spectrum with that of the starting material revealed the loss of the angular methyl group and the appearance of a singlet at $\tau = 4{\cdot}95$. The structure VIII is proposed for this product which is formed from the initial oxime undergoing firstly 7–20 ether formation which finds a ready analogy in the reactions[3,4] of ajaconine, and subsequently the lactone undergoes internal hydrolysis and lactamization to form the system reminiscent of the diterpene alkaloids. Thus this reaction forms an exception to the currently accepted six-membered transition state theory for the Barton reaction.

EXPERIMENTAL

M.ps were determined on a Kofler block. Alumina for chromatography was acid-washed Grade III; light petroleum refers to the fraction b.p. 60–80°. Solutions were dried over Na_2SO_4. Unless otherwise stated IR spectra were determined for Nujol mulls and NMR spectra were obtained in $CDCl_3$ solution with a Varian Associates A60 spectrometer using tetramethylsilane as internal standard.

Oxidation of 6α,7α-*dihydroxy*-(—)-*kauran*-19-*oic acid* 19–6α-*lactone* (IVa) *with iodine and lead tetra-acetate*

The hydroxy-lactone[2] (400 mg), I_2 (730 mg) and lead tetra-acetate (750 mg) in benzene (30 ml) were irradiated under reflux under N_2 for 3 hr. The solution was poured into water and extracted with ether. The extract was washed with $Na_2S_2O_3$aq, $NaHCO_3$aq, water and dried. Recovery gave 7α,20-*epoxy*-6α-*hydroxy*-(—)-*kauran*-19-*oic acid* 19 → 6α-*Lactone* (Va; 275 mg) which crystallized from acetone–light petroleum as needles, m.p. 195–196°. (Found: C, 75·5; H, 8·6. $C_{20}H_{28}O_3$

---

[17] D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *J. Amer. Chem. Soc.* **82**, 2640 (1960); **83**, 476 (1961); A. L. Nussbaum and C. H. Robinson, *Tetrahedron* **17**, 35 (1962).

[18] A. Gaudenier, J. Polonsky and E. Wenkert, *Bull. Soc. Chim.* 407 (1964).

requires: C, 75·9; H, 8·9%.) ν_{max} 1765 cm^{-1}. The IR spectrum of the crude product showed the presence of traces of the corresponding 7-ketone.

The lactone was recovered unchanged after 5 hr from attempted hydrolysis with refluxing methanolic 1N NaOHaq.

Reduction of the ether (Va)

The ether (190 mg) and LAH (200 mg) in a mixture of ether (10 ml) and tetrahydrofuran (5 ml) were left at room temp overnight. Dil. HCl acid was added and the solution extracted with ether. The extract was washed with NaHCO$_3$aq, water, dried and evaporated to give *7α,20-epoxy-6α,19-dihydroxy-(−)-kaurane* (120 mg) which crystallized from acetone—light petroleum as needles, m.p. 158–160°. (Found: C, 74·5; H, 9·9. $C_{20}H_{32}O_3$ requires: C, 75·0; H, 10·1%), ν_{max} 3180 (sh), 3100 cm^{-1}.

Oxidation of 7α,20-epoxy-6α,19-dihydroxy-(−)-kaurane

The diol (75 mg) in acetone (10 ml) was treated with the 8N CrO$_3$ reagent[19] at room temp overnight. MeOH was added, the solution concentrated, diluted with water and extracted with ether. The extract was washed with water, dried and evaporated. *7α,20-Epoxy-6-oxo-(−)-kauran-19-oic acid* (lactonol form; 35 mg) crystallized as needles from acetone-light petroleum, m.p. 226–228°. (Found: C, 71·9; H, 8·4. $C_{20}H_{28}O_4$ requires: C, 72·3; H, 8·5%), ν_{max} 3300, 1770 cm^{-1}.

Reduction of the lactonol

The above lactonol (25 mg) in ether (10 ml) and tetra-hydrofuran (5 ml) was treated with LAH (100 mg) at room temp overnight. The solution was treated dropwise with water and then poured into dil HCl and extracted with ether. Recovery gave 7α,20-epoxy-6α-hydroxy-(−)-kauran-19-oic acid 19 → 6α-lactone (8 mg) m.p. 194–195°, identified by its IR spectrum.

Reduction of methyl 7-oxo-(−)-kaur-16-en-19-oate (VIa)

The keto-ester[8] (360 mg) in MeOH (10 ml) was treated with NaBH$_4$ (200 mg) at room temp for 2 hr. The solution was acidified, concentrated, poured into water and extracted with ether. Recovery gave a crystalline residue which was chromatographed on alumina. Elution with 40% ether–light petroleum gave *methyl 7α-hydroxy-(−)-kaur-16-en-19-oate* (VIb; 240 mg) as needles, m.p. 145–146°. (Found: C, 75·7; H, 9·8. $C_{21}H_{32}O_3$ requires: C, 75·9; H, 9·7%), ν_{max} 3588, 1728, 1650, 875 and 368 cm^{-1}.

Oxidation of the alcohol with lead tetra-acetate and iodine in benzene under irradiation as described earlier gave mainly intractable material from which a low yield of methyl 7-oxo-(-)-kaur-16-en-19-oate was recovered.

Reduction of 6α-hydroxy-7-oxo-18-nor-(−)-kaur-16-en-19-oic acid 19 → 6α-lactone (III)

The keto-lactone (III; 940 mg; from 7,18-dihydroxy-kaurenolide, 1·5 g) in MeOH (15 ml) and dioxan (5 ml) was treated with NaBH$_4$ (500 mg) at room temp for 1 hr. Dil. HCl (1 ml) was added and the MeOH and dioxan removed *in vacuo*. The solution was diluted with NH$_4$Claq and extracted with ethyl acetate. The extract was washed with NaHCO$_3$aq, water and dried. Recovery afforded *6α,7α-dihydroxy-(−)-18-norkaur-16-en-19-oic acid 19 → 6α-lactone* (690 mg) which crystallized from acetone–light petroleum as needles, m.p. 209–211°. (Found: C, 75·9; H, 8·9. $C_{19}H_{26}O_3$ requires: C, 75·5; H, 8·7%), ν_{max} 3540, 1762, 1658, and 895 cm^{-1}.

Hydrogenation of 6α,7α-dihydroxy-(−)-18-norkaur-16-en-19-oic acid 19 → 6α-lactone

10% Pd–C (100 mg) suspended in ethyl acetate (50 ml) was saturated with H$_2$ and then the lactone (650 mg) in ethyl acetate (150 ml) was added and the mixture shaken. One mole H$_2$ was absorbed rapidly. Recovery gave a solid which after several recrystallizations, from acetone–light petroleum gave *6α,7α-dihydroxy-16-epi-(−)-18-norkauran-19-oic acid 19 → 6α-lactone* (IVb; 300 mg) as needles, m.p. 189–190°. (Found: C, 74·9; H, 9·1. $C_{19}H_{28}O_3$ requires: C, 75·0; H, 9·3%), ν_{max} 3510, 1760 cm^{-1}.

---

[19] R. G. Curtis, Sir I. Heilbron, E. R. H. Jones, and C. F. Woods, *J. Chem. Soc.* 457 (1953).

Hydrogenation of 7,18-*dihydroxykaurenolide* (VII)

10% Pd–C (500 mg) suspended in ethyl acetate (100 ml) was saturated with H_2 and then the kaurenolide (3 g) in ethyl acetate (200 ml) was added and the mixture shaken until the rapid uptake of H_2 ceased. Recovery gave a solid which was recrystallized from acetone–light petroleum as needles of β-dihydro 7,18-dihydroxy kaurenolide, m.p. 223–224°.[5]

Preparation of the toluene-p-*sulphonates of* 7,18-*dihydroxy kauranolide*

7,18-Dihydroxykauranolide (250 mg) was treated with toluene-*p*-sulphonyl chloride (650 mg) in freshly purified pyridine (2 ml) at room temp for 2 days. The mixture was poured into dil HCl and the product recovered in ethyl acetate and chromatographed on alumina. Elution with 10% ether–light petroleum gave the *ditoluene*-p-*sulphonate* of 7,18-dihydroxykauranolide (71 mg) which crystallized from light petroleum as prisms, m.p. 194–195°. (Found: C, 63·6; H, 6·4. $C_{34}H_{42}O_8S_2$ requires: C, 63·5; H, 6·6%), ν_{max} 1782, 1603 cm^{-1}.

Further elution with 60% ether–light petroleum gave the 18-*mono-toluene*-p-*sulphonate* of β-dihydro 7,18-dihydroxy kaurenolide (130 mg) which crystallized from acetone–light petroleum as needles, m.p. 205–206°. (Found: C, 66·3; H, 7·2. $C_{27}H_{36}O_6S$ requires C, 66·4; H, 7·4%), ν_{max} 3550, 1770 and 1600 cm^{-1}.

Reductions with lithium aluminium hydride

(a) The 18-monotoluene-*p*-sulphonate of β-dihydro-7,18-dihydroxykaurenolide (102 mg) in ether (10 ml) and dioxan (5 ml) was treated with LAH (104 mg) overnight. Ethyl acetate followed by dil HCl was cautiously added and the solution extracted with ethyl acetate. The extract was washed with $NaHCO_3$aq, water and dried. Recovery gave a gum which was chromatographed on alumina. Elution with 9:1 ether: MeOH gave 6α,7β,19-*trihydroxy*-16-epi-(−)-*kaurane* (35 mg) which crystallized as needles from aqueous MeOH, m.p. 246–247°. (Found: C, 73·9; H, 10·6; $C_{20}H_{34}O_3$ requires: C, 74·5; H, 10·6%), ν_{max} 3300 (br) cm^{-1}.

(b) 7-Hydroxykauranolide[2] (100 mg) was reduced with LAH (120 mg) in ether: dioxan (30 ml) as above, to give the identical (by IR and mixed m.p.) triol (63 mg).

(c) Methyl 6α.7α-dihydroxy-(−)-kaur-16-en-19-oate[2] (75 mg) in dry ether (25 ml) and LAH (100 mg) were heated under reflux for 1·5 hr. The solution was cooled and the excess reagent destroyed with ethyl acetate and the organic material recovered in ether. 6α,7α,19-*trihydroxyl*-(−)-*kaur*-16-*ene* (55 mg) crystallized from acetone–light petroleum as needles, m.p. 211–213°. (Found: C, 73·4; H, 10·2. $C_{20}H_{32}O_3 \cdot 0{\cdot}5H_2O$ requires: C, 72·9; H, 10·1%), ν_{max} 3480, 3220, 1655 and 870 cm^{-1}.

Oxidation of the kauranolide

β-Dihydro-7,18-dihydroxykaurenolide (1·3 g) in acetone (50 ml) was treated with the 8N CrO_3 reagent (3 ml) at room temp for 3 hr. MeOH was added, the solution concentrated and heated with water on a steambath for 1 hr. The product was recovered in ethyl acetate and crystallized from acetone–light petroleum to give 6α-*hydroxy*-7-*oxo*-16-epi-(−)-18-*norkauran*-19-*oic acid* 19 → 6α-*lactone* (1·01 g) as prisms, m.p. 162–163°. (Found: C, 74·9; H, 8·9. $C_{19}H_{26}O_3$ requires: C, 75·5; H, 8·7%), ν_{max} 1775 and 1705 cm^{-1}.

Reduction of the keto-lactone

The keto-lactone (900 mg) in tetrahydrofuran (25 ml) and MeOH (15 ml) was treated with $NaBH_4$ (250 mg) for 3·5 hr. The solution was acidified and concentrated *in vacuo*. It was diluted with NH_4Claq and extracted with ethyl acetate. The extract was washed with $NaHCO_3$aq, dried and evaporated to give IVb (0·53 g) which crystallized from acetone–light petroleum as needles, m.p. 189–191° identical with the material prepared above.

Oxidation of 6,7-*dihydroxy*-16-epi-(−)-18-*norkauran*-19-*oic acid* 19 → 6-*lactone with iodine and lead tetra-acetate*

The hydroxy-lactone (180 mg), I_2 (210 mg) and lead tetra-acetate (300 mg) in benzene (25 ml) were irradiated under reflux under N_2 for 3 hr. The solution was poured into water and extracted with ether. The extract was washed with $Na_2S_2O_3$aq, $NaHCO_3$aq, water and dried. Recovery gave 7α,20-*epoxy*-6α-*hydroxy*-16-epi-(−)-18-*norkauran*-19-*oic acid* 19 → 6α-*lactone* (Vb) which crystallized from acetone–light petroleum as needles, m.p. 207–208°. (Found: C, 74·9; H, 8·5. $C_{19}H_{26}O_3$ requires: C, 75·5; H, 8·7%). ν_{max} 1770 cm^{-1}.

Photolysis of the nitrite of 6α,7α-*dihydroxy*-(−)-18-*norkauran*-19-*oic acid* 19 → 6-*lactone*

The hydroxy-lactone (350 mg) was treated with excess nitrosyl chloride in pyridine (3 ml) at −10° for 15 min. The solution was poured into ice-water and rapidly worked up in ether. The extract was washed several times with ice-cold water, dried and evaporated at room temp. The residue was dissolved in benzene and irradiated under N_2 with water cooling for 0·5 hr. The benzene was evaporated and the residual gum in isopropanol (10 ml) heated under reflux for 1 hr. The solvent was evaporated and the residue chromatographed on silica gel. Elution with 40% ether–light petroleum gave 6-hydroxy-7-oxo-(−)-18-nor-kauran-19-oic acid 19 → 6-lactone (20 mg) identified by its IR spectrum. Subsequent elution with ether: MeOH gave the *lactam* (VIII; 190 mg), m.p. 243–244°. (Found: C, 69·0; H, 8·4. $C_{19}H_{27}O_4N$ requires: C, 68·4; H, 8·16%), ν_{max} 3490, 3140 (br), 1640 cm^{-1}.

Acknowledgement—I wish to thank Professor D. H. R. Barton, F.R.S. for his interest and encouragement in this work and I.C.I. Ltd. (Pharmaceuticals Division) for the gift of some chemicals.