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THE COMPLETE STRUCTURE OF ABBEOKUTONE

J. R. HANSON and A. F. WHITE
School of Molecular Sciences, University of Sussex, Brighton, BN1 9QJ, Sussex

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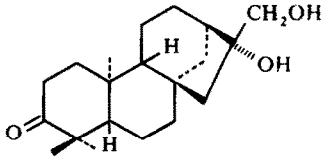
Abstract—The carbonyl group of abbeokutone is located on ring A by the formation of a bromo-αβ-unsaturated ketone containing the chromophore O=C.C(Br)=CH.C and at position 3 by the formation of a seco-acid containing the grouping CH_2=C.(CH_3). The 16α-hydroxyl stereochemistry is confirmed by its formation from 3α-hydroxy- and 3-oxo-(−)-kaur-16-ene.

ABBEOKUTONE has been assigned[2] the structure I. In connection with our studies[3] on the biosynthesis of the gibberellins, we required (−)-kaurene stereospecifically labelled with tritium at various positions on ring A. Abbeokutone was a potential source of (−)-kaurene labelled at position 3. However, although abbeokutone had been correlated with (−)-kaurane, the location of the CO group was not proven. Through the courtesy of Professor D. A. H. Taylor, we have completed this aspect of abbeokutone chemistry.

On treatment with acetic anhydride in pyridine, abbeokutone formed a monoacetate at room temperature and a diacetate on refluxing. Comparison of the NMR spectrum of the monoacetate with that of abbeokutone (τ CH_2OH 6·27, CH_2OAc 5·75) showed that the primary alcohol was acetylated first. Both gave the corresponding equatorial alcohols (τ CH·OH 6·7 and 6·8) on reduction with sodium borohydride. The diacetoxy-mono-ol formed a toluene-*p*-sulphonate. This gave a *cis* disubstituted olefin (τ 4·59 2H, ν_{max} 735 cm^{-1} cf lup-2-ene,[4] 730 cm^{-1}) on refluxing with collidine which is in accord with a methylene ketone in abbeokutone. Bromination of the monoacetate with excess bromine in acetic acid followed by dehydrobromination with lithium bromide and lithium carbonate in DMF, gave a monobromo-αβ-unsaturated ketone. The NMR spectrum of this showed one olefinic proton at τ 2·47 as a singlet which was assigned to the β-proton of an αβ-unsaturated ketone. The UV spectrum showed λ_{max} 258 nm in accord[5] with the fragment O=C·C(Br)=CH·C. The only kauranoid positions available for a CO group which would afford this chromophore are positions 1 and 3. These positions were distinguished by the following reaction. The monoacetate of abbeokutone was treated with *m*-chloroperbenzoic acid. After extensive chromatography, a carboxylic acid was obtained. This showed NMR resonances at τ 8·25(3), 5·30(1) and 5·12(1) together with only one saturated C—CH_3 resonance at τ 8·98. Thus two of the three Me groups of abbeokutone have been replaced by the grouping CH_2=C(CH_3). Consequently the CO group of abbeokutone is located at position 3 and the acid has the structure II.

Abbeokutone was reduced with sodium borohydride to a triol which was oxidized with sodium periodate to give a 17-norketone. Treatment of this with methylene triphenyl phosphorane gave (−)-kaur-16-en-3α-ol which had identical physical constants to material reported[7] by Jefferies. Furthermore oxidation of the kaurenol



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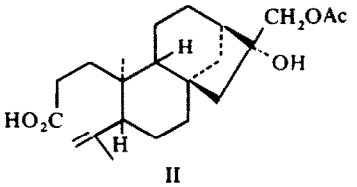

II

to 3-oxo-(−)-kaur-16-ene and hydroxylation with osmium tetroxide regenerated abbeokutone. Osmylation is a reaction that is known to afford the 16α-hydroxyl stereochemistry.[8] A second sequence also provided confirmation of this stereochemistry. Abbeokutone formed a monotoluene-*p*-sulphonate in which the primary alcohol was acylated (τ 5·83). Reduction of this with LAH gave (−)-kauran-3α,16α-diol. The same diol was prepared by epoxidation of (−)-kaur-16-en-3α-ol and reduction of the epoxide with LAH. Epoxide formation like osmylation in the kaurene series, occurs from the α-face of the molecule.

EXPERIMENTAL

General experimental details have been described previously.[9] The abbeokutone had m.p. 190–191° and was a gift from Professor D. A. H. Taylor.

Acetylation of abbeokutone. Abbeokutone (500 mg) on treatment with Ac_2O (0·5 ml) in pyridine (10 ml) overnight gave a *monoacetate*, m.p. 136–137°. (Found: C, 73·0; H, 9·15. $C_{22}H_{34}O_4$ requires: C, 72·9; H, 9·45%); τ 9·00(3), 8·93(6), 7·96(3), 5·72(2); ν_{max} 3450, 1735, 1690 cm^{-1}. Abbeokutone (350 mg) on refluxing with Ac_2O (0·5 ml) in pyridine (5 ml) or with NaOAc for 2 hr, gave a diacetate, m.p. 125–126° (lit,[2] m.p. 127–129°). (Found: C, 70·8; H, 8·95. Calc for $C_{24}H_{36}O_5$: C, 71·25; H, 9·0%); τ 9·00(3), 8·93(6), 8·03(3), 7·97(3), 5·60(1) and 5·07(1) (J = 13 Hz); ν_{max} 1735, 1720 and 1700 cm^{-1}.

Reduction of the acetates. The keto-acetates (200 mg) in MeOH (10 ml) were treated with $NaBH_4$ (100 mg) for 2 hr. The solns were poured into water and the products filtered and recrystallized from aqueous MeOH. 16α,17-*Diacetoxy-(−)-kauran-3α-ol* crystallized as needles, m.p. 174–175°. (Found: C, 69·9; H, 9·5. $C_{24}H_{38}O_5\frac{1}{2}H_2O$ requires: C, 69·4; H, 9·4%); τ 9·23(3), 9·03(3), 8·99(3), 8·03(3), 7·95(3), 6·78(1)(m), 5·55(1) and 5·07(1) (J = 13 Hz); ν_{max} 3400 (br), 1735, 1720 cm^{-1}. 17-*Acetoxy-(−)-kauran-3α,16α-diol* crystallized as needles, m.p. 218–220°. (Found: C, 72·2; H, 9·7. $C_{22}H_{36}O_4$ requires: C, 72·5; H, 9·95%); τ 9·24(3), 9·06(3), 9·00(3), 7·90(3), 5·75(2), 6·7(1) (m); ν_{max} 3550, 3450 (br), 1710 cm^{-1}.

16α,17-*Diacetoxy-(−)-kaur-2-ene.* The 3α-*toluene-p-sulphonate* of 16α,17-diacetoxy-(−)-kauran-3α-ol was prepared with toluene-*p*-sulphonyl chloride in pyridine. It crystallized from light petroleum as needles, m.p. 159–160°. (Found: C, 66·7; H, 8·3. $C_{31}H_{44}SO_7$ requires: C, 66·4; H, 7·9%); τ 9·20(6), 9·00(3), 8·04(3), 7·98(3), 7·56(3), 5·78(1) (q 7·10 Hz), 5·56(1) and 5·04(1) (J = 13 Hz), 2·64(2) and 2·16(2) (J = 8 Hz); ν_{max} 1735, 1720 and 1600 cm^{-1}. The toluene-*p*-sulphonate (150 mg) was heated under reflux with collidine (10 ml). The soln was cooled, poured onto ice-cold 2N HCl and the product recovered in AcOEt. Chromatography on alumina gave in the fractions eluted with light petroleum, 16α,17-*diacetoxy-(−)-kaur-2-ene*, which crystallized from MeOH as prisms, m.p. 136–137°. (Found: C, 74·25; H, 8·8. $C_{24}H_{36}O_4$ requires: C, 74·2; H, 9·3%); τ 9·12(3), 9·06(3), 8·96(3), 8·03(3), 7·95(3), 5·56(1) and 5·05(1) (J = 13 Hz), 4·59(2); ν_{max} 1735, 1720, 735 cm^{-1}.

Bromination of abbeokutone acetate. Bromine (4·5 g) in AcOH (32 ml) containing NaOAc (2·3 g) was added dropwise to a soln of the acetate (4·8 g) in AcOH (32 ml) containing 44% HBr (0·15 ml). The soln was poured onto ice and the ppt collected, washed with $NaHCO_3$ aq, dissolved in ether and dried over anhyd K_2CO_3. Recovery gave a gum which was refluxed with LiCl (3·5 g) and Li_2CO_3 (2 g) in DMF (75 ml)

under N_2 for 4 hr. Ether was added and the soln washed with H_2O, dil HCl, $NaHCO_3$aq, dried and evaporated. Chromatography on silica gave in the fractions eluted with 50–70% AcOEt–light petroleum, 17-*acetoxy*-2-*bromo*-16α-*hydroxy*-3-*oxo*-(−)-*kaur*-1-*ene* (0·87 g), which crystallized from AcOEt–light petroleum as needles, m.p. 171–174°. (Found: C, 60·3; H, 7·2. $C_{22}H_{31}O_4Br$ requires: C, 60·1; H, 7·1%); τ 8·82(6), 8·70(3), 7·88(3), 5·72(2), 2·47(1); ν_{max} 3510, 1730, 1680, 1603 cm^{-1}; λ_{max} 258 nm (MeOH).

Cleavage of ring A. Abbeokutone monoacetate (750 mg) in $CHCl_3$ (10 ml) was treated with *m*-chloroperbenzoic acid (2 g) for 2 days at room temp. The soln was diluted with $CHCl_3$, washed with $FeSO_4$aq, dil HCl, $NaHCO_3$aq, dried and evaporated. The residual gum was chromatographed three times on silica in 15% AcOEt–light petroleum to give 17-*acetoxy*-16α-*hydroxy*-3,4-*seco*-(−)-*kaur*-4(18)-*en*-3-*oic acid* (95 mg) which crystallized from acetone–light petroleum as needles, m.p. 77–78°. (Found: C, 69·2; H, 9·4. $C_{22}H_{34}O_5$ requires: C, 69·8; H, 9·05%); τ 8·98(3), 8·25(3), 7·90(3), 5·75(2), 5·30(1), 5·12(1); ν_{max} 3400 (br), 1735, 1710, 890 cm^{-1}.

3α-*Hydroxy*-(−)-*kaur*-16-*ene*. This was arepared by a procedure similar to that recorded by Jefferies *et al.*[7] It crystallized from light petroleum as needles, m.p. 170° (lit,[7] 172–173°). (Found: C, 83·3; H, 11·1. Calc for $C_{20}H_{32}O$: C, 83·3; H, 11·2%); ν_{max} 3390, 1660, 880 cm^{-1}. The *toluene*-p-*sulphonate* had m.p. 143°. (Found: C, 73·5; H, 8·8. $C_{27}H_{38}SO_3$ requires: C, 73·2; H, 8·7%). Oxidation of the alcohol with the 8N CrO_3 reagent gave 3-oxo-(−)-kaur-16-ene which crystallized from aqueous MeOH as needles, m.p. 87–88·5° (lit,[7] 88–88·5°). (Found: C, 78·95; H, 10·1. Calc for $C_{20}H_{30}O\frac{1}{2}H_2O$: C, 78·9; H, 10·1%); ν_{max} 1698, 1660, 899 cm^{-1}.

Abbeokutone. 3-Oxo-(−)-kaur-16-ene (75 mg) in ether (5 ml) was treated with OsO_4 (100 mg) in pyridine (3 ml) for 16 hr. The soln was poured into $NaHSO_3$aq and allowed to stand for 2 hr. Recovery in AcOEt gave abbeokutone (35 mg), m.p. 190°, identical (IR) with an authentic sample.

3α,16α-*Dihydroxy*-(−)-*kaurane*

(i) Abbeokutone, on treatment with toluene-*p*-sulphonyl chloride in pyridine at room temp for 18 hr, formed a 17-*monotoluene*-p-*sulphonate*, m.p. 139–140°. (Found: C, 68·0; H, 7·6. $C_{27}H_{38}SO_5$ requires: C, 68·3; H, 8·1%); τ 9·00(3), 8·94(6), 7·55(3), 5·83(2), 2·63(2) and 2·13(2) (J = 9 Hz); ν_{max} 3470, 1690, 1600 cm^{-1}. The monotoluene-*p*-sulphonate (110 mg) in ether (10 ml) was heated under reflux with LAH (500 mg) for 4 hr. The soln was diluted with moist ether and washed with dil HCl. Recovery and chromatography on alumina gave 3α,16α-*dihydroxy*-(−)-*kaurane* which crystallized from acetone as needles, m.p. 168–170°. (Found: C, 78·7; H, 10·9. $C_{20}H_{34}O_2$ requires: C, 78·4; H, 11·2%); τ 9·22(3), 9·04(3), 9·00(3), 8·66(3), 6·83(1) (m); ν_{max} 3350 (br) cm^{-1}.

(ii) 3α-Hydroxy-(−)-kaur-16-ene (150 mg) in $CHCl_3$ (10 ml), was treated with *m*-chloroperbenzoic acid (200 mg) overnight. The soln was diluted, washed with $FeSO_4$aq, dil HCl, $NaHCO_3$aq, dried and evaporated. Chromatography gave 16α-17-*epoxy*-(−)-*kauran*-3α-*ol* which crystallized from light petroleum as needles, m.p. 154–157°. (Found: C, 78·7; H, 10·1. $C_{20}H_{32}O_2$ requires: C, 78·9; H, 10·6%); τ 9·22(3), 9·02(3), 8·95(3), 7·17(2) (q J = 4, 6 Hz), 6·8(1), (q J = 7, 10 Hz); ν_{max} 3300 (br) cm^{-1}. The epoxide (50 mg) in ether (5 ml) was heated with LAH (200 mg) for 3 hr. The soln was diluted with moist ether, washed with dil HCl and the product recovered. 3α,16α-Dihydroxy-(−)-kaurane crystallized from acetone as needles, m.p. 167–169°, identical (IR) with the sample obtained above.

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