# The Stereochemistry of Migrated Hopanes Epimeric at C-21

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The structures of four migrated hopanes, isolated from *Sorghum bicolor* and epimeric at C-21 and/or enantiomeric at the C-8, C-13, C-14, C-17, C-18, and C-21 positions: fernenol, 21-epifernenol (trematol), isoarborinol, and 21-epi-isoarborinol (sorghumol, a previously unidentified pentacycle), have been determined by analysing the chromatographic (g.l.c. and h.p.l.c.), spectral (mass and $^{1}$H n.m.r.), and physical constant (m.p.) data of the naturally occurring (free) and chemically synthesized acetate and methyl ether derivatives.

The co-occurrence of pairs of triterpenoids which are either epimeric at C-20 (tetracyclic triterpenoids) or C-21 (pentacyclic triterpenoids) is rare, but known in some plants *e.g.*, euphol and 20-epieuphol (tirucallol[1,2]), and fern-9-ene and 21-epifern-9-ene.[3] Diastereoisomeric pairs[4—8] such as euphol and lanosterol, and fernenol and isoarborinol occur more commonly. To our knowledge, no plant has been shown to produce a cyclase(s) that converts squalene or its epoxide into a complete stereochemical series of triterpenoid products in which the molecules of the series possess both an epimeric and antipodal (with respect to the C/D and D/E ring junctions) steric arrangement of the ring systems *e.g.*, as in the series: euphol, tirucallol, lanosterol, and 20-epilanosterol. We have now isolated such a series.

From an acetone extract[†] of flowering *Sorghum bicolor* cv.

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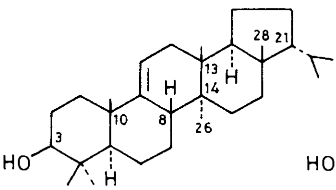
[†] The methods by which we isolated, separated, and identified these pentacyclic triterpenoids were the same as previously described for sterols. R. C. Heupel and W. D. Nes, *J. Nat Prod.*, in the press; W. D. Nes and A. E. Stafford, *Proc. Natl. Acad. Sci. USA*, 1982, **80**, 3227.

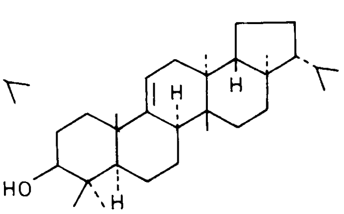
6499 GBR we obtained four pentacyclic chiral molecules that are stereochemically varied in the C, D, and E rings and possess an asymmetric isopropyl substituent attached to C-21. Three of the four compounds were found to be the known migrated hopanes fernenol (**2**), trematol (**3**), and isoarborinol (**4**). The fourth is a new compound, which we call by the trivial name, sorghumol (**1**). Sorghumol was found to be the only migrated hopane produced by another variety of *S. bicolor* (cv. IS809) and its synthesis was demonstrated by the use of [2-$^{14}$C]-acetate.

Comparison of the electron impact mass (e.i. m.s.) and 200 MHz $^1$H n.m.r. spectra and chromatographic data of the isolated compounds, their methyl ethers, and acetates (either as pure compounds or as mixtures, depending on the variety of *Sorghum* from which they were isolated) with the reported migrated hopane literature[4—12] confirmed the identity of the three known compounds. Just as (**2**) is the C-21 epimer of (**3**), from the physical properties of (**1**) it appears that this compound is the C-21 epimer of (**4**).

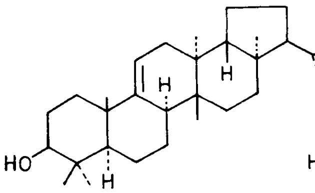
The e.i. m.s. of the new compound was similar to that of the other three.[4—8] However, we observed that (**1**) possessed a diagnostic enhanced molecular ion [$M^+$ (94%), $M^+-$Me (100%), inlet source temperature 140 °C] which the other compounds lacked [$M^+$ ($\leqslant$70%), $M^+-$Me (100%)]. The melting points of compounds (**1**) (277—282 °C) and (**2**) (lit.[9] 192—193 °C) were *ca.* 20 °C lower than those of their respective C-21 epimers (**4**) (lit.[9] 295—300 °C) and (**3**). On reversed phase h.p.l.c., developed with 96% aq. MeOH, (**1**) separated from (**4**) by a factor of 1.07 which is analogous to the other epimeric pair. On g.l.c. (3% OV-17, 235 °C), (**1**) has a longer elution time (RRTc 2.92, retention relative to cholesterol) than (**4**) (RRTc 2.26). Conversely, (**2**) (RRTc 224) elutes before (**4**), while (**3**) (RRTc 3.18) elutes substantially later, as expected.[12]



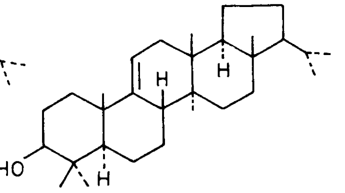
Sorghumol
(**1**)



Fernenol
(**2**)



Trematol
(**3**)



Isoarborinol
(**4**)

$^1$H N.m.r. decoupling experiments performed on each of the four migrated hopanes identified the two methyl doublets and indicated that they were associated with an isopropyl group, not a 1,2-dimethyl (C-19 and C-20) substituted E ring as in migrated ursanes such as baurenol. The chemical shifts of the isopropyl methyls and the coupling constants were identical (*cf.* Table 1) in all four compounds.

In order to assign the other peaks corresponding to the methyl proton resonances at C-23, C-24, C-25, C-26, C-27, and C-28, we examined the chemical shifts upon acetylation and methylation and in certain cases performed a shift reagent study [using tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-octane-4,6-dionato)europium(III), Eu(fod)$_3$], on the free alcohols (data not shown). In support of the results of Barton *et al.*[3] for the desoxy migrated hopane pair, fern-9-ene and 21-epifern-9-ene, we observed that the chemical shifts of the ring A methyl group protons occur at progressively lower field in the order 4α > 4β > 10β, rather than 4β > 4α > 10β as reported for other pentacyclic triterpenoids.[13,14] While the n.m.r. data (60 and 100 MHz) obtained in the earlier studies[6,9—11] were inconclusive with regard to stereochemical considerations, we observed that inversion of the configuration at C-21 causes a similar shift of the C-26 signal in the two sets of epimeric pairs, (**1**)–(**4**) and (**2**)–(**3**). Specifically, when the C-28 methyl group signal was originally *cisoid* and then considered *transoid* to the isopropyl group, a downfield (δ *ca.* 0.080) shift of the C-26 signal occurs. Another downfield shift, but in the diastereoisomeric pairs (**1**)–(**3**) and (**2**)–(**4**) of δ *ca.* 0.025 for the C-28 signal, occurs following simultaneous inversion at C-8, C-13, C-14, C-17, C-18, and C-21. Conformational differences that result from inversion also affect the location of the vinyl proton absorption signal (*cf.* Table 1). The demonstrable differences in the various properties of the

**Table 1.** Methyl assignments [$^1$H n.m.r. (200 MHz) δ (CDCl$_3$)] of migrated hopanes isolated from *Sorghum bicolor*.

| Methyl substituent at C- | 3β-OH[a] | | | | 3β-OMe | | | | 3β-OAc | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | (**1**) | (**2**) | (**3**) | (**4**) | (**1**) | (**2**) | (**3**) | (**4**) | (**1**) | (**2**) | (**3**) | (**4**) |
| 4α | 0.984 | 0.963 | 0.965 | 1.002 | 0.965 | 0.948 | 0.945 | 0.984 | 0.862 | 0.844 | 0.845 | 0.881 |
| 4β | 0.814 | 0.871 | 0.855 | 0.799 | 0.796 | 0.847 | 0.834 | 0.781 | 0.886 | 0.940 | 0.926 | 0.870 |
| 10β | 0.765 | 0.758 | 0.746 | 0.763 | 0.764 | 0.757 | 0.745 | 0.766 | 0.761 | 0.749 | 0.767 | 0.766 |
| 14α | 1.032 | | | 0.950 | 1.031 | | | 0.948 | 1.054 | | | 0.969 |
| 14β | | 1.066 | 0.989 | | | 1.061 | 0.988 | | | 1.084 | 0.989 | |
| 13α | | 0.812 | 0.892 | | | 0.811 | 0.895 | | | 0.804 | 0.890 | |
| 13β | 0.806 | | | 0.950 | 0.804 | | | 0.948 | 0.803 | | | 0.949 |
| 17α | | 0.731 | 0.731 | | | 0.729 | 0.731 | | | 0.727 | 0.737 | |
| 17β | 0.756 | | | 0.758 | 0.755 | | | 0.757 | 0.754 | | | 0.756 |
| 29[b] | 0.829 | 0.829 | 0.828 | 0.829 | 0.828 | 0.829 | 0.828 | 0.829 | 0.829 | 0.827 | 0.828 | 0.827 |
| 30[b] | 0.889 | 0.889 | 0.900 | 0.889 | 0.889 | 0.889 | 0.900 | 0.889 | 0.889 | 0.887 | 0.900 | 0.889 |

[a] The C-11 proton resonance was observed as a quartet in each case δ 5.25 (**1**), 5.31 (**2**), 5.37 (**3**), and 5.31 (**4**). [b] (d, *J* 6.5 Hz). Assignments may be reversed.

four migrated hopanes are thus related to the stereochemistry of the ring system and of the isopropyl group attached to C-21.

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