Conversion of a Simple Meliacin (7α-Acetoxymeliaca-14,20,22-trien-3-one) into Azadirone and of Khayanthone into Khivorin

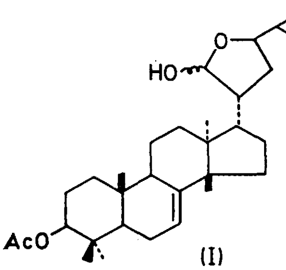
By J. G. ST. C. BUCHANAN and T. G. HALSALL*
(*The Dyson Perrins Laboratory, University of Oxford, Oxford* OX1 3QY)

Summary The simple meliacin (IIa) (7α-acetoxymeliaca-14,20,22-trien-3-one) has been converted into azadirone (IIb) by treatment with copper(II) bromide followed by dehydrobromination; khayanthone (IV) has been converted into khivorin (V) by oxidation with alkaline hydrogen peroxide followed by re-acetylation.

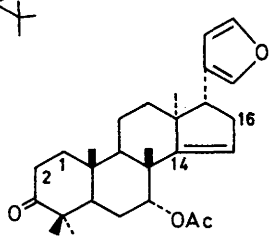
RECENTLY[1] we have described the partial synthesis from turraeanthin (I) of the simple meliacin (IIa). This has now been converted into a naturally-occurring compound. Treatment of (IIa) with copper(II) bromide in tetrahydrofuran solution and dehydrobromination of the resulting bromo-ketone (IIc) with 1,5-diazabicyclo[4,3,0]non-5-ene gave in 71% overall yield azadirone (IIb), $[\alpha]_D + 24°$ (lit. value[2] $+26°$) with the expected i.r., n.m.r., and mass spectral properties.

One of the characteristic features of many of the more highly oxygenated meliacins and limonoids is the ring-D $\alpha\beta$-epoxy-δ-lactone system exemplified by limonin,[3] gedunin,[4] and khivorin (V).[5] It has been suggested[3] that this arises biogenetically by the further oxidation of the D-ring in structures such as (IIa) and (IIb) which have been suggested as intermediates in the earlier stages of the biosynthetic pathway. Three oxidative steps are needed, allylic oxidation at C-16 [*cf.* (IIa) to (III)], epoxidation of the Δ^{14}-double bond, and Baeyer–Villiger lactone formation from the 16-keto derivatives [*cf.* (IV) to (V)]. So far the only one of these carried out chemically has been the oxidation[2] of azadirone (IIb) by selenium dioxide to give the corresponding 16-ketone, azadiradione (III). This step, together with the above result represents a formal synthesis of azadiradione (III) from turraeanthin (I). A further step in the elaboration of the more highly oxygenated structures has now been accomplished: the formation of the epoxy-lactone system with the conversion of khayanthone (IV)[6] into khivorin (V).

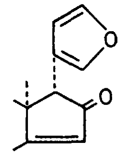
Khayanthone (IV) in t-butyl alcohol and 7% 4N-sodium hydroxide solution was treated with hydrogen peroxide (20% of 30%) and stirred for 5 days at 40°. Re-acetylation of the resulting product yielded khivorin (V), m.p. and mixed m.p., 257—259°, $[\alpha]_D -42°$, in 40% yield. None of the isomeric 15,16-*seco*-compound was detected.



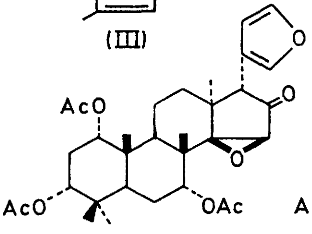
(I)



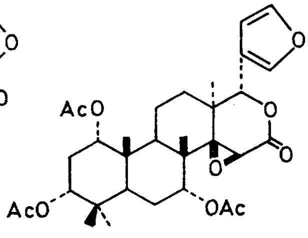
(IIa)
(IIb) 1,2-dehydro-(IIa)
(IIc) 2α-bromo-(IIa)



(III)



(IV)



(V)

We thank Professor D. A. H. Taylor for a generous gift of khayanthone.

(*Received, November 4th,* 1969; *Com.* 1667.)

---

[1] J. G. St. C. Buchanan and T. G. Halsall, *Chem. Comm.*, 1969, 48 and 242.

[2] D. Lavie and M. K. Jain, *Chem. Comm.*, 1967, 278.

[3] D. Arigoni, D. H. R. Barton, E. J. Corey, O. Jeger, L. Caglioti, Sukh Dev, P. G. Ferrini, E. R. Glazier, A. Melera, S. K. Pradhan, K. Schaffner, F. Sternhell, J. F. Templeton, and F. Tobinga, *Experientia*, 1960, **16**, 41.

[4] A. Akisanya, C. W. L. Bevan, T. G. Halsall, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.*, 1961, 3705; S. A. Sutherland, G. A. Sim, and J. M. Robertson, *Proc. Chem. Soc.*, 1962, 222.

[5] E. K. Adesogan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1967, 554.

[6] E. K. Adesogan and D. A. H. Taylor, *Chem. Comm.*, 1967, 379.