Vaalens Sesquiterpenes of *Catha transvaalensis*; Structure of Vaalens-5 using the COLOC N.m.r. Pulse Sequence

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Catha transvaalensis (Celastraceae), a rare relative of *Catha edulis* which is the source of the psychotomimetic drug khat, contains at least six related extractives. The major member of the group, vaalens-5, is shown with the help of the n.m.r. pulse sequence COLOC to be the 1,6-diacetyl-9-(*E*)-cinnamoyl-1,4,6,9,15-pentahydroxydihydroagarofuran (**1**).

Catha edulis (Vahl.) Forssk. ex Endl. (khat or quat) is an important psychotomimetic or stimulant plant [1] which has long been used in the Arabian peninsula, Africa, and Madagascar. In recent times the practice of chewing the leaves and young twigs has increased considerably, causing concern to the U.N. Division of Narcotic Drugs. Until 1966 the plant was thought to be the sole member of the genus *Catha* Forssk. ex Scop. but in that year a new species confined to a relatively small area of N.E. Transvaal was identified and at first placed in a new genus as *Lydenburgia cassinoides* N. K. B. Robson, but later reclassified as *Catha transvaalensis* Codd.[2] Very recently a third rare species *Catha abbotti* Van Wyk and Prins, occurring in S. Natal/Pondoland, has also been described.[3]

In previous work we have made an extensive study of the alkaloidal sesquiterpenes which occur in khat [4] and through the kindness of Professor van Wyk of the University of Pretoria it has been possible for us to examine a specimen of the leaves and young twigs of *Catha transvaalensis*. The ground plant material was extracted with methanol and the extracts were diluted with water and partitioned into benzene. The benzene was evaporated and the product was chromatographed on Florisil with gradient elution (ethyl acetate 15% increasing to 75%, in hexane) monitoring with Dragendorff reagent. Colours were much weaker than those with khat, but fractions showing colour were united and separated by h.p.l.c. (silica, ethyl acetate–hexane). This gave four discrete compounds, with a further two in admixture (see Table). Spectroscopic information indicates that all are related in type, and we now report on the structure of the major compound vaalens-5.

Table. The vaalens extractives from *Catha transvaalensis*

	Molecular formula	*M*	M.p. (°C)
Vaalens-1	$C_{28}H_{36}O_8$	500	214—218
Vaalens-3	$C_{32}H_{40}O_{12}$	616	79—82
Vaalens-5	$C_{28}H_{36}O_9$	516	195—197
Vaalens-7	$C_{30}H_{38}O_{11}$	574	181—183

Vaalens-5, $C_{28}H_{36}O_9$, contained two acetates [$M^+ - 42$ and $M^+ - 60$; δ_H 1.52 (s, 3 H) and 2.12 (s, 3 H); δ_C 25.7, 21.6, 172.5, and 170.4], one (*E*)-cinnamate [$M^+ - 148$; δ_H 6.35 (d, *J* 16 Hz, 1 H), 7.68 (d, 1 H), 7.4 (m, 3 H), and 7.54 (m, 2 H); δ_C 166.0 (CO), 117.5 and 146.0 (C=C), and 134.2, 128.3, 128.9, and 130.6 (Ph)], one primary hydroxy [δ_H 3.93 (2 H), 2.36 (t, *J* 5.5 Hz, OH, D_2O exchg.)], and one tertiary hydroxy [δ_H 2.91 (D_2O exchg.)].

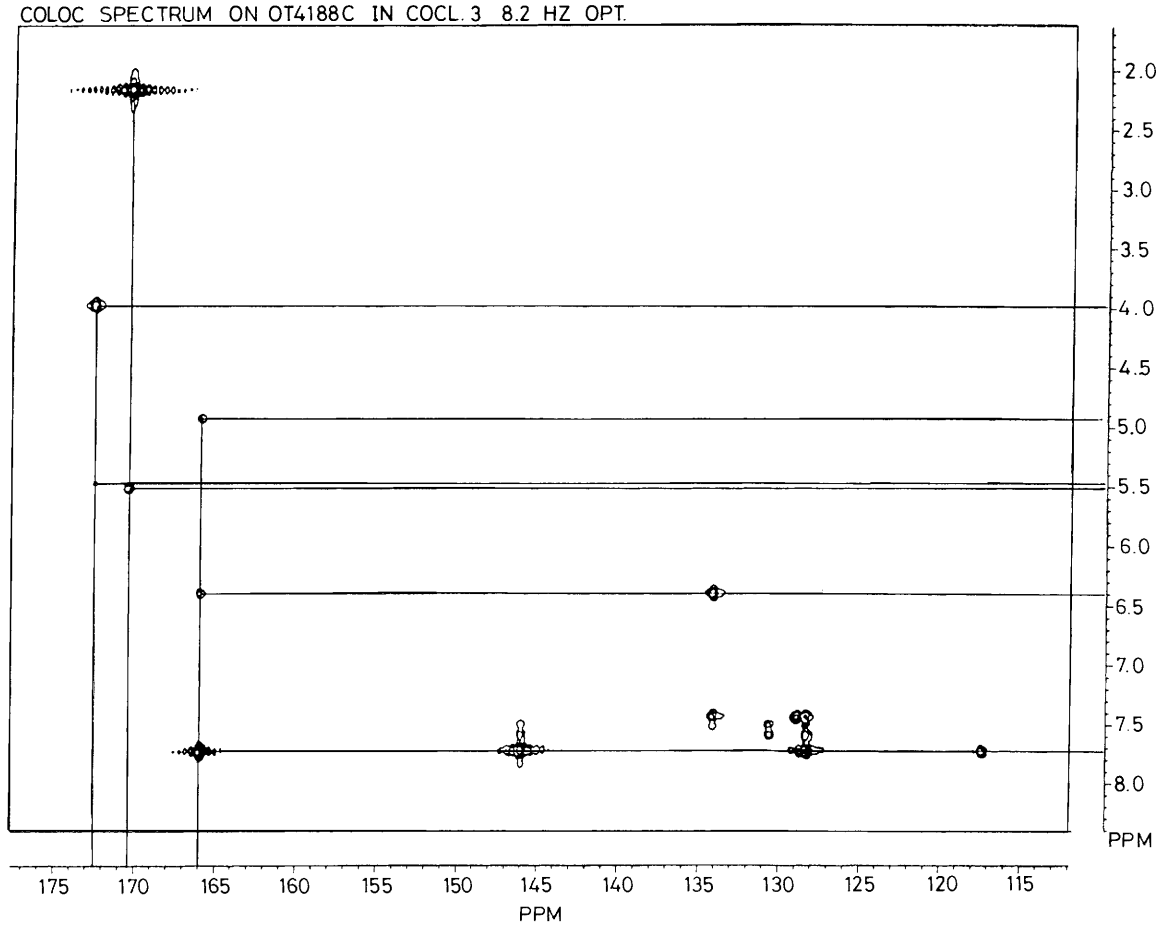


Figure 1. Portion of the COLOC diagram for vaalens-5

The remaining ^{1}H n.m.r. signals were consistent with those expected of a dihydroagarofuran core and this is confirmed by a complete assignment of the ^{13}C n.m.r. signals and by comparison with literature data.[4–7] The dihydroagarofuran skeleton comprises a *trans*-fused chair-chair decalin distorted by a 1,3-diaxial bridge: the geometry therefore departs from ideal in a way which is reflected by J_{vic} around the ring and is of assistance in placing the oxygenated functions on the core. Thus RCO_2 functions may be placed at C-1, C-6, and C-9 through location of 1-$H_{ax.}$ [5.43 (d, $J_{1a,2a}$ 12.3, $J_{1a,2e}$ 4.1 Hz), 9-$H_{eq.}$ [4.88 (d, $J_{8e,9a}$ 6.8, $J_{8e,9e}$ ~0 Hz] and 6-$H_{ax.}$ [5.46 (s, $J_{6a,7e}$ ~0 Hz]. One CH_3CO, δ 1.52 shows shielding and this would be consistent with a 1-OAc (eq.), 9-OCOAr (ax.) arrangement leading to a 1,6-diacetoxy-9-cinnamoyloxy substitution. The ^{13}C resonances at 60.8 and 70.4 allow placement of the two hydroxy groups at C-15 and C-4 in accordance with literature precedent.

This tentative assembly was now confirmed by heteronuclear shift correlation *via* small coupling constants with broad-band decoupling in t_1 (COLOC).[8] A key portion (C-sp^2) of the spectrum is shown in Figure 1 along with a selection of correlations (at *J* 8.2 Hz) in Figure 2. Some key connections are as follows: (a) 1-H (5.43) to acetate *C*O (172.5) and to *C*-10 (51.4); also *C*O (172.5) to 15-H_2: this confirms the siting of the acetate and the 15-OH; (b) 9-H (4.88) to cinnamate *C*O (166.0) (the latter also links to the cinnamyl hydrogens, thus confirming the proposed assignments and sitings); (c) 6-H (5.46) to acetate *C*O (170.4) and to C-11; and (d) tertiary-OH (2.91) to C-14. This leads to the structure shown in Figure 2, or formula (**1**) in projection form.

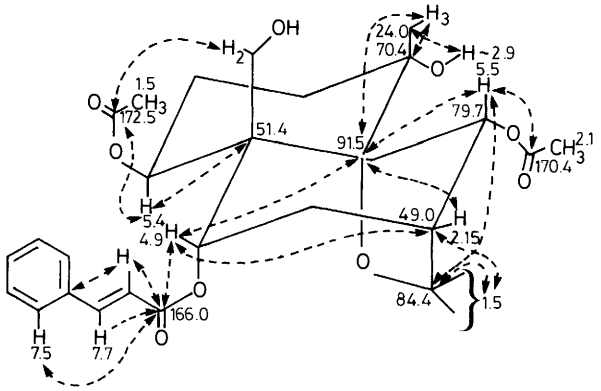
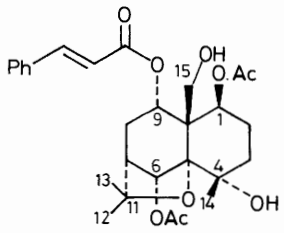
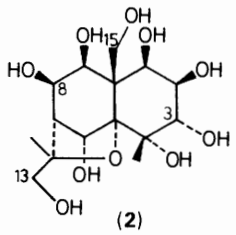


Figure 2. A section of ^{1}H, ^{13}C long-range connectivities for vaalens-5

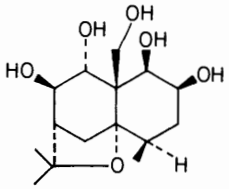
In comparing vaalens-5 with khat alkaloids[4] it must be borne in mind that the latter are only alkaloids because nitrogenous acids esterify a hydroxylated dihydroagarofuran core such as euonyminol (**2**). The medium molecular weight (750—900) khat alkaloids (cathedulins-K1, -K2, -K6, and -K15) and higher molecular weight (1 000—1 200) khat alkaloids (cathedulins-E3, -E4, -E6, -K12, -K17, -K19, and -K20) have complex structures by virtue of esters formed from dibasic acids spanning 8-$OH_{ax.}$ and 15-OH, and 3-$OH_{ax.}$ and 13-OH. Smaller khat alkaloids such as cathedulins-E2 and -E8 (molecular weight 700 and 595) are based on the sesquiterpene core (**3**) and may be



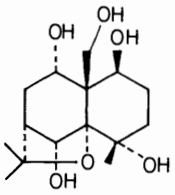
(1)



(2)



(3)



(4)

compared with the vaalens-5 core (**4**). Esters of variously hydroxylated dihydroagarofurans are characteristic of the Celastraceae in general but we have not encountered cinnamic acid as an esterifying acid in the khat alkaloids, though it is found esterified in other Celastraceae dihydroagarofurans.

Acknowledgements

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