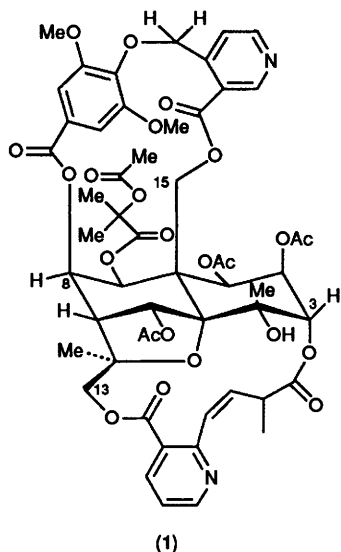


## Isolation and Structure of Vaalens-1, -3, -5, and -7. Sesquiterpene Esters of *Catha Transvaalensis* Codd (Celastraceae): X-Ray Molecular Structure of Vaalens-5

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Four sesquiterpene esters are isolated from *Catha transvaalensis*, a rare relative of *Catha edulis* which is the source of the Middle Eastern drug Khat. The structure of one of these esters, vaalens-5, including its absolute configuration, is unequivocally determined by single-crystal X-ray analysis, correcting an earlier proposal: the lattice contains two distinct conformers, distortions being caused by hydrogen bonding. Vaalens-1, -3, and -7 are also assigned structures. Chemotaxonomic relationships between the two species are not close.

The plant drug Khat or Quat from *Catha edulis* (Vahl.) Forsk. ex Endl (Celastraceae) is used as a stimulant, particularly in parts of Arabia, East Africa, and Madagascar.<sup>1</sup> (-)-Cathinone is the major active principle, acting very like (+)-amphetamine, though there are few reports of amphetamine-like psychotic states developing after consumption of Khat, probably because the large amounts of plant material that must be chewed makes the activity self-limiting. Our interests have been in the structures of the higher molecular weight cathedulin alkaloids ( $M$  600–1 200) which Khat contains, cathedulin-K 19 (1) being a typical example.<sup>2</sup> Some fourteen cathedulin alkaloids have now been isolated, and they are all based on highly hydroxylated sesquiterpene (dihydroagarofuran) cores variously esterified by acids, some of which (cathic, edulinic, evoninic, nicotinic) are nitrogen-containing, thus permitting the cathedulins to be classified as alkaloids.<sup>2</sup>



For a long time, *Catha edulis* was thought to be the sole member of the genus *Catha* Forsk., but in more recent times a new species has been described and classified as *Catha transvaalensis* Codd, after being earlier placed in a new genus on its own as *Lydenburgia cassinoides* N. K. B. Robson.<sup>3</sup> It is known only in a limited area of northeastern Transvaal and very recently a third rare species, occurring in south Natal/Pondoland, has been described and named *Catha abbotti*

Table 1. Sesquiterpene ester extractives from *Catha transvaalensis*.

	Formula	Accurate mass (EI) <sup>a</sup>	$M^+$ (FAB) <sup>d</sup>	M.p. (°C)
Vaalens-1	C <sub>28</sub> H <sub>36</sub> O <sub>8</sub>	440.2194 (+0.4) <sup>b</sup>	501.2488	214–218
Vaalens-5	C <sub>28</sub> H <sub>36</sub> O <sub>9</sub>	516.2355 (+0.4)	517.2438	195–197
Vaalens-7	C <sub>30</sub> H <sub>38</sub> O <sub>11</sub>	574.2404 (+0.7)	575.2492	181–183
Vaalens-3	C <sub>32</sub> H <sub>40</sub> O <sub>12</sub>	574.2355 (-4.2) <sup>c</sup>	617.2598	79–82

<sup>a</sup> As measured, with deviation from calculated in mmu in parentheses. <sup>b</sup>  $M - \text{AcOH}$ . <sup>c</sup>  $M + 1 - \text{Ac}$ . <sup>d</sup>  $M + 1$ , peak matched.

Van Wyk and Prins.<sup>4</sup> Through the kindness of Professor Van Wyk we have been able to examine a specimen of the dried leaves and twigs of *Catha transvaalensis* for sesquiterpene ester alkaloids which might resemble those of the cathedulin group.

Ground *C. transvaalensis* was solvent-extracted, and the extract was examined by gradient elution chromatography, *via* monitoring with Dragendorff's reagent to detect alkaloid-containing fractions. It was found, however, that Dragendorff colours were much weaker than those experienced during Khat extractions. Nevertheless all fractions showing Dragendorff colours were amalgamated and subjected to further separation using HPLC on silica with ethyl acetate-hexane mixtures as eluant. As indicated in Table 1 four compounds, all nitrogen free, were isolated pure and named vaalens-1, -3, -5, and -7, together with two further non-nitrogenous compounds not yet obtained pure.

The structure of vaalens-5, the major extractive, was determined by single-crystal X-ray analysis using a crystal grown in methanol-water. Despite the presence of two crystallographically independent molecules, the structure was solved by direct methods using diffractometer data and refined to  $R$  3.44% over 4 897 independent reflections. Figures 1 and 2 show the conformations of these two molecules in the crystal, representing formula (2). The absolute configuration was also determined using careful measurement of Friedel pairs, and was found to agree with that deduced for neoevonine (as determined by the heavy-atom method using the bromoacetyl derivative of its monohydrate).<sup>5</sup> The X-ray numbering scheme is displayed in Figure 3 and bond lengths and angles are listed in Tables 2 and

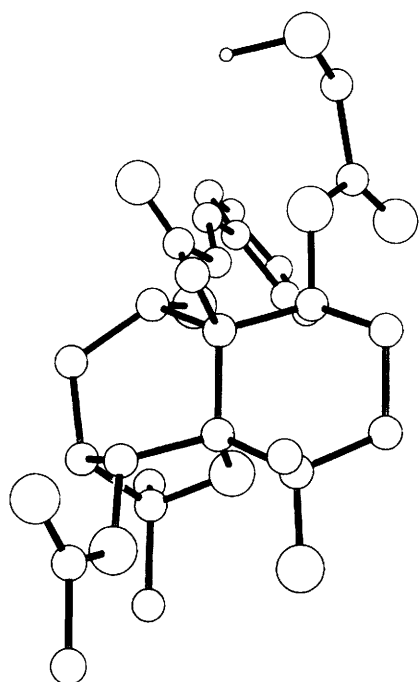


Figure 1. X-ray structure of vaalens-5 in conformation A.

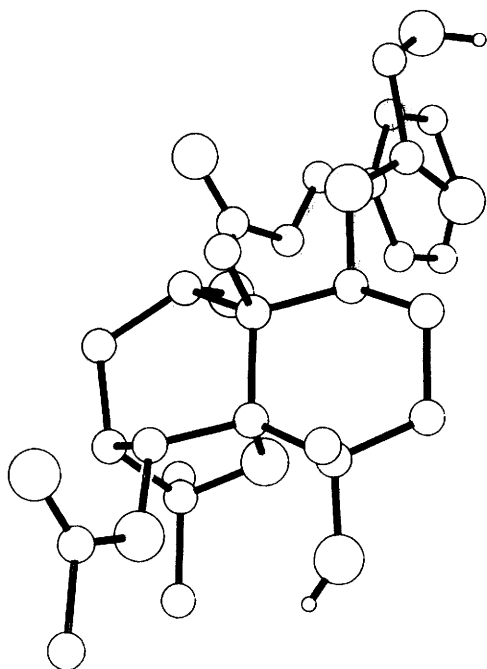


Figure 2. X-ray structure of vaalens-5 in conformation B.

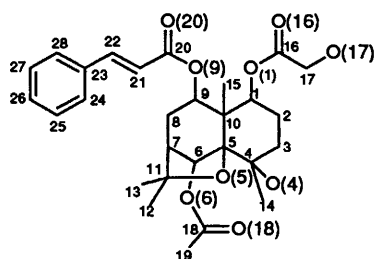


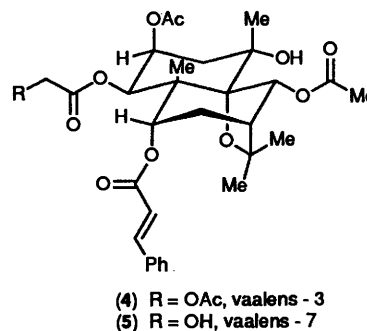
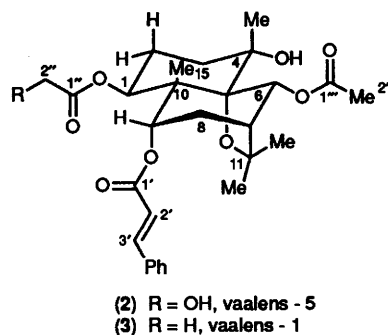
Figure 3. X-ray numbering scheme for vaalens-5.

Table 2. Bond lengths (Å) for vaalens-5 with standard deviations in parentheses.

	Mol. (A)	Mol. (B)		Mol. (A)	Mol. B
C(1)–C(2)	1.513(4)	1.510(4)	C(11)–C(13)	1.541(4)	1.538(5)
C(1)–C(10)	1.532(3)	1.540(3)	C(11)–O(5)	1.472(3)	1.462(3)
C(1)–O(1)	1.462(3)	1.458(3)	C(16)–C(17)	1.512(5)	1.513(4)
C(2)–C(3)	1.521(4)	1.516(5)	C(16)–O(1)	1.322(3)	1.332(3)
C(3)–C(4)	1.529(4)	1.532(5)	C(16)–O(16)	1.193(4)	1.190(3)
C(4)–C(5)	1.570(3)	1.570(4)	C(17)–O(17)	1.396(5)	1.390(4)
C(4)–C(14)	1.538(4)	1.527(5)	C(18)–C(19)	1.487(5)	1.503(5)
C(4)–O(4)	1.431(3)	1.429(4)	C(18)–O(6)	1.326(3)	1.325(4)
C(5)–C(6)	1.541(3)	1.535(4)	C(18)–O(18)	1.200(4)	1.190(5)
C(5)–C(10)	1.572(3)	1.572(3)	C(20)–C(21)	1.468(4)	1.475(4)
C(5)–O(5)	1.450(3)	1.454(3)	C(20)–O(9)	1.347(3)	1.350(3)
C(6)–C(7)	1.521(4)	1.522(4)	C(20)–O(20)	1.197(4)	1.201(4)
C(6)–O(6)	1.442(3)	1.443(3)	C(21)–C(22)	1.311(4)	1.331(4)
C(7)–C(8)	1.542(4)	1.547(4)	C(22)–C(23)	1.463(4)	1.463(4)
C(7)–C(11)	1.536(4)	1.533(4)	C(23)–C(24)	1.391(5)	1.395(4)
C(8)–C(9)	1.533(4)	1.538(4)	C(23)–C(28)	1.389(4)	1.395(4)
C(9)–C(10)	1.556(3)	1.559(4)	C(24)–C(25)	1.372(5)	1.376(5)
C(9)–O(9)	1.454(3)	1.455(3)	C(25)–C(26)	1.348(5)	1.378(6)
C(10)–C(15)	1.545(3)	1.549(4)	C(26)–C(27)	1.374(6)	1.382(6)
C(11)–C(12)	1.516(4)	1.530(5)	C(27)–C(28)	1.382(6)	1.375(6)

3, respectively, together with their standard deviations: the latter adopt expected values. The conformation of the central six-membered ring systems, with the ether bridge sharpening the chair at C(6), and flattening it at C(9), is very similar to that encountered in 'Ever-1'.<sup>6</sup>

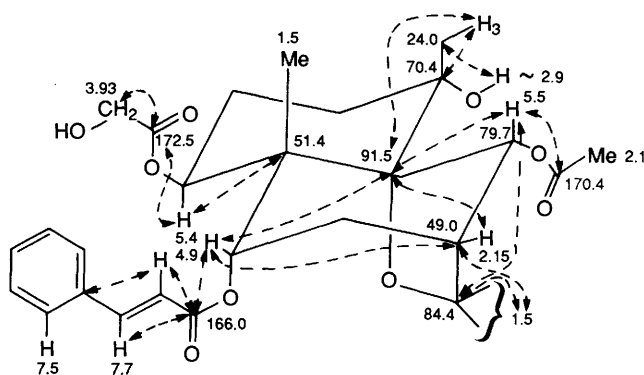
Both alcohol functions were found to form hydrogen bonds in the crystal structure, and these explain the two crystallographically independent molecules and the conformational differences between them. The length and angle data associated with the hydrogen bonds are shown in Table 4. Both glycolic hydroxy groups [O(17)] of the conformational pair form strong intermolecular hydrogen bonds with their complementing partner—one to the cinnamate carbonyl O(20), one to the acetate carbonyl O(18). However, in order to form these bonds the conformation about the C(16)–C(17) bond has to be



**Table 3.** Bond angles (°) for vaalens-5 with standard deviations in parentheses.

	Mol. (A)	Mol. (B)
C(2)-C(1)-C(10)	113.3(2)	112.9(2)
C(2)-C(1)-O(1)	110.4(2)	111.3(2)
C(10)-C(1)-O(1)	106.2(2)	106.0(2)
C(1)-C(2)-C(3)	108.1(2)	107.7(3)
C(2)-C(3)-C(4)	113.6(2)	113.6(3)
C(3)-C(4)-C(5)	109.6(2)	110.3(2)
C(3)-C(4)-C(14)	111.0(2)	110.0(3)
C(3)-C(4)-O(4)	107.9(2)	107.1(3)
C(5)-C(4)-C(14)	114.5(2)	115.1(3)
C(5)-C(4)-O(4)	109.0(2)	107.7(3)
C(14)-C(4)-O(4)	104.4(2)	106.2(3)
C(4)-C(5)-C(6)	117.4(2)	118.1(2)
C(4)-C(5)-C(10)	113.8(2)	114.7(2)
C(4)-C(5)-O(5)	105.4(2)	105.1(2)
C(6)-C(5)-C(10)	107.0(2)	106.4(2)
C(6)-C(5)-O(5)	104.8(2)	104.9(2)
C(10)-C(5)-O(5)	107.7(2)	106.8(2)
C(5)-C(6)-C(7)	99.8(2)	100.1(2)
C(5)-C(6)-O(6)	112.8(2)	114.0(2)
C(7)-C(6)-O(6)	111.0(2)	111.7(2)
C(6)-C(7)-C(8)	105.1(2)	105.1(2)
C(6)-C(7)-C(11)	102.8(2)	102.6(2)
C(8)-C(7)-C(11)	114.6(2)	114.4(2)
C(7)-C(8)-C(9)	116.4(2)	115.6(2)
C(8)-C(9)-C(10)	114.9(2)	114.8(2)
C(8)-C(9)-O(9)	108.9(2)	110.2(2)
C(10)-C(9)-O(9)	109.9(2)	109.1(2)
C(1)-C(10)-C(5)	108.2(2)	108.3(2)
C(1)-C(10)-C(9)	109.8(2)	110.1(2)
C(1)-C(10)-C(15)	109.7(2)	109.8(2)
C(5)-C(10)-C(9)	110.4(2)	110.2(2)
C(5)-C(10)-C(15)	113.0(2)	113.2(2)
C(9)-C(10)-C(15)	105.6(2)	105.3(2)
C(7)-C(11)-C(12)	115.6(2)	115.1(3)
C(7)-C(11)-C(13)	113.6(2)	113.9(3)
C(7)-C(11)-O(5)	101.5(2)	101.6(2)
C(12)-C(11)-C(13)	107.4(2)	107.6(3)
C(12)-C(11)-O(5)	109.8(2)	109.3(3)
C(13)-C(11)-O(5)	108.7(2)	109.0(3)
C(17)-C(16)-O(1)	112.5(3)	109.5(2)
C(17)-C(16)-O(16)	122.7(3)	125.5(3)
O(1)-C(16)-O(16)	124.8(3)	125.0(3)
C(16)-C(17)-O(1)	115.9(3)	114.0(3)
C(19)-C(18)-O(6)	110.2(3)	111.3(4)
C(19)-C(18)-O(18)	126.3(3)	125.6(4)
O(6)-C(18)-O(18)	123.6(3)	123.1(3)
C(21)-C(20)-O(9)	109.8(3)	109.7(2)
C(21)-C(20)-O(20)	125.9(3)	125.9(2)
O(9)-C(20)-O(20)	124.3(3)	124.4(3)
C(20)-C(21)-C(22)	123.4(3)	119.8(3)
C(21)-C(22)-C(23)	126.5(3)	126.9(3)
C(22)-C(23)-C(24)	122.5(3)	122.9(3)
C(22)-C(23)-C(28)	120.0(3)	119.6(3)
C(24)-C(23)-C(28)	117.4(3)	117.4(3)
C(23)-C(24)-C(25)	122.2(3)	121.1(3)
C(24)-C(25)-C(26)	119.6(4)	120.8(4)
C(25)-C(26)-C(27)	119.3(4)	118.9(4)
C(26)-C(27)-C(28)	120.8(4)	120.6(3)
C(23)-C(28)-C(27)	120.7(4)	121.2(4)
C(1)-O(1)-C(16)	117.8(2)	117.3(2)
C(5)-O(5)-C(11)	111.0(2)	111.0(2)
C(6)-O(6)-C(18)	119.1(2)	118.2(2)
C(9)-O(9)-C(20)	118.4(2)	118.4(2)

modified in the two molecules. In molecule A, O(17) is close to eclipsing O(1), while in molecule B it is close to eclipsing the carbonyl O(16). Similarly, the cinnamate hydrogen-bond acceptor in molecule B causes the carbonyl O(20) to be twisted

**Figure 4.** A selection of  $^1\text{H}$ - $^{13}\text{C}$  long-range connectivities for vaalens-5.**Table 4.** Hydrogen bonds in vaalens-5.

		O...O	H...O	O-H...O
O(4) Mol. (A)	O(16) Mol. (A) (-x, y - 1/2, 1 - z)	3.18	2.65	126.1
	O(5) Mol. (A)	2.68	2.12	128.5
O(4) Mol. (B)	O(6) Mol. (B)	2.86	2.58	103.6
O(17) Mol. (A)	O(20) Mol. (B) (x, 1 + y, z)	2.95	1.69	164.9
O(17) Mol. (B)	O(18) Mol. (A) (1 - x, y - 1/2, 1 - z)	2.78	1.95	153.2

20° out of conjugation with the double bond, whereas the cinnamate group is planar and in full conjugation in molecule A. It is only in these two regions of the molecule that any significant differences are to be found in the bond length and angle data between molecules A and B in Tables 2 and 3. The tertiary alcohol O(4) forms a weak bifurcated inter- and intra-molecular hydrogen bond in molecule A, and a different intramolecular hydrogen bond in molecule B as shown in Table 4. However, both of these interactions are energetically too small to disturb the conformation of the molecules.

The X-ray structure differs from that previously proposed on the basis of NMR data in that the hydroxy group originally positioned at C-15 must be repositioned on the methyl of the C-1 acetoxy, the latter becoming a glycolate ester.<sup>7</sup> Modification of the  $^1\text{H}$ - $^{13}\text{C}$  long-range connectivity diagram (COLOC)<sup>8</sup> is required as shown in Figure 4 (see ref. 7 for the COLOC diagram).

Relative to vaalens-5, vaalens-1 lacks a single oxygen atom, though NMR data show that in other respects it is very similar structurally to the former. The appearance of a new acetyl group ( $\delta_{\text{H}}$  1.83;  $\delta_{\text{C}}$  21.0) (Tables 5 and 6) makes it clear that it is the 2'-oxygen that is absent; thus vaalens-1 has structure (3).

Relative to vaalens-5, vaalens-3 has one additional acetyl group and a new acetoxy residue as shown by its molecular formula and new  $^1\text{H}$  NMR signals at  $\delta$  1.87 and 2.06 as well as new  $^{13}\text{C}$  NMR signals at  $\delta_{\text{C}}$  169.8 and 169.9. There is no spectral evidence of acetylation at the hindered tertiary hydroxy group at C-4, which is normally found free in this type of Celastraceous sesquiterpene. One acetyl is placed on the hydroxy group of the C-1 glycolate residue [the hydroxy resonance (t) near  $\delta$  2.36 has disappeared], whilst the second acetyl is placed as an acetoxy residue at C-2 which has undergone a  $^{13}\text{C}$  shift from  $\delta_{\text{C}}$  23.6 in vaalens-5 to  $\delta_{\text{C}}$  68.5 in vaalens-3. The  $^1\text{H}$  signal at C-2 is a multiplet, but the coupling to the C-1 axial hydrogen can be seen as a doublet of  $J$  4.1 Hz, demonstrating that the new acetoxy group at C-2 is axial (see Table 7). Vaalens-3 is thus formulated as having structure (4)

Relative to vaalens-3, vaalens-7 lacks one acetyl moiety and this, and the  $^1\text{H}$  and  $^{13}\text{C}$  data (Tables 5-7), show that vaalens-7

**Table 5.**  $^1\text{H}$  NMR spectra ( $\delta$ ,  $\text{CDCl}_3$ ).

H	Vaalens-1 (3)	Vaalens-5 (2)	Vaalens-7 (5)	Vaalens-3 (4)
1-H <sub>a</sub>	5.33dd	5.43dd	5.57obs	5.59d
2-H <sub>c</sub>			5.51m	5.49m
6-H <sub>a</sub>	5.47s	5.46s	5.57s	5.57s
7-H <sub>c</sub>		2.15obs		2.1–2.2obs
8-H <sub>c</sub>	2.42m	2.4obs	2.45m	2.46m
9-H <sub>c</sub>	4.85d	4.88d	4.83d	4.74d
4-OH	2.90s	2.91s	3.00s	2.96s
2''-OH		2.36t	2.39t	
2''-H <sub>2</sub>		3.93ddd	3.91d	4.39dd
2'-H	6.39d	6.35d	6.34d	6.33d
3'-H	7.69d	7.68d	7.68d	7.67d
5', 9'-H	7.4br m	7.4br m	7.4br m	7.4br m
6', 7', 8'-H	7.55br m	7.55br m	7.55br m	7.55br m
C-Me	1.32,	1.32,	1.48,	1.48,
	1.35,	1.35,	1.51,	1.50,
	1.50,	1.52,	1.53,	1.50,
	1.52	1.53	1.55	1.54
COMe	1.83			1.87
	2.13	2.12	2.03,	2.06,
			2.12	2.14

**Table 6.**  $^{13}\text{C}$  NMR spectra ( $\delta$ ,  $\text{CDCl}_3$ ).

C	Vaalens-1 (3)	Vaalens-5 (2)	Vaalens-7 (5)	Vaalens-3 (4)
1	72.7*	73.9	72.1	72.4*
2	23.6	23.6	68.6	68.5
3	38.5	38.4	42.1	42.0
4	70.4	70.4	69.9	69.8
5	91.5	91.5	91.3	91.3
6	79.8	79.7	79.2	79.3
7	49.1	49.0	49.1	49.0
8	31.8	31.9	31.3	31.2
9	72.3*	72.4	72.1	71.1*
10	51.3	51.4	51.4	51.3
11	84.3	84.4	84.8	84.8
12	19.6	19.5	21.1	20.1
13	21.6	21.6	21.5	21.6
14	24.0	24.0	25.3	25.3
15	25.7	25.7	25.8	25.7
1'	165.9	166.0	165.9	165.8
1''	170.1†	172.5	172.4	169.6†
1'''	170.4†	170.4	170.3	170.3
2'	117.9	117.5	117.4	117.7
3'	145.6	146.0	146.2	146.0
4'	134.4	134.2	134.2	134.4
5',9'	128.0	127.5	128.4	128.3
6',8'	128.3	128.5	128.9	128.8
7'	130.4	130.6	130.6	130.4
2''	21.0	60.8	60.6	60.4
2'''	29.7	29.7	29.7	29.7
CO			169.9	169.9†,
				169.8†

Assignments which may be interchanged vertically are indicated \* or †.

**Table 7.** Selected  $J_{gem}$ - and  $J_{vic}$ -values.

H-H	$J(\text{Hz})$	H-H	$J(\text{Hz})$
1a-2a	12.3 <sup>a</sup>	8e-7e	4.1 <sup>b</sup>
1a-2e	4.1 <sup>a</sup>	8a-8e	12.1 <sup>b</sup>
6a-7e	~0 <sup>a</sup>	2''H <sub>A</sub> -2''H <sub>B</sub>	15.6 <sup>c</sup>
8e-9e	6.8 <sup>a</sup>	2''H <sub>2</sub> -OH	5.5 <sup>b</sup>
8a-9e	~0 <sup>a</sup>	2'-3'	16.0 <sup>b</sup>

<sup>a</sup> Vaalens-5. <sup>b</sup> Vaalens-1. <sup>c</sup> Vaalens-3. Similar  $J$ -values were measured for parallel H-H relationships in each ester, though in some instances they were obscured.

must have structure (5) with the free glycolate hydroxy group appearing at  $\delta_{\text{H}}$  2.39 (t): there was no evidence of environmental change in the vicinity of other acyl groups.

As a group, the vaalens sesquiterpene esters lack the 13-hydroxy and axial 3-hydroxy groups on the core which are necessary for the evoninic diester bridge to be formed in order to belong to the medium molecular weight (700–900) group of Khat alkaloids which contains cathedulins K1, K2, K6, and K15.<sup>2</sup> Apart from this requirement for an evoninic or edulinic diester bridge, the larger Khat alkaloids [cathedulins E3, E4, E6, K12, K17, K19(1), and K20] additionally require hydroxylation at C-15 and C-8<sub>ax</sub> to provide for the cathate span and neither of these positions is hydroxylated in the vaalens series. There are also differences between the hydroxylation pattern of the vaalens series (1<sub>eq</sub>, 2<sub>ax</sub>, 4<sub>eq</sub>, 6<sub>eq</sub>, and 9<sub>ax</sub>) and the smaller Khat alkaloids, cathedulins E2 and E8 (molecular weight 700 and 595) which have 1<sub>eq</sub>, 2<sub>ax</sub>, 8<sub>ax</sub>, 9<sub>ax</sub>, and 15-hydroxylation.<sup>2</sup> In contrast to the Khat alkaloids none of the vaalens compounds investigated has nitrogen-containing esterifying groups. The glycolate esterification is a distinctly unusual feature and the cinnamate esterifying residue has also not been found in the Khat alkaloids, though it is found in other dihydroagarofuran cores from the Celastraceae family.<sup>9</sup> Esterified dihydroagarofurans are fairly commonly found in the latter family,<sup>9</sup> so from a phytochemical point of view there are no close connections between *Catha edulis* and *C. transvaalensis*.

## Experimental

**Extraction of *Catha transvaalensis*.**—Dry ground leaves and twigs (1.3 kg) were stirred with methanol (7 l) for 2 days at room temperature. The extract was filtered and concentrated (1.2 l), diluted with water (1.2 l), and extracted with benzene (1 × 1.5 l, then 3 × 1 l). Evaporation of the benzene below 40 °C then gave an extractive (76 g). One half of this extractive was dissolved in chloroform–hexane (1:1) and chromatographed on Florisil (60–100 mesh; 250 g), and eluted sequentially first with ethyl acetate–hexane (1:9) (1 l), followed by (1:4) (2 l), (1:1) (1.5 l), and (3:1) (1 l), then with ethanol–ethyl acetate (1:19) (1.5 l) and (1:1) (1 l); fractions (250 ml) were collected. All the fractions (12–18) giving a red colour with Dragendorff's reagent were combined and evaporated (1.83 g).

The combined fractions were now separated by preparative HPLC on silica using a Waters Prep LC 500 equipment and ethyl acetate–hexane (7:3) as eluant. The individual fractions were now further purified using a Waters S-15 silica (2 cm × 25 cm) semi-preparative column. The pure samples were crystallised from ethyl acetate–hexane. Further details are given in Table 1.

**Crystallographic Analysis of Vaalens-5.**—Crystal data:  $\text{C}_{28}\text{H}_{36}\text{O}_9$ ;  $M = 516.60$ ; Monoclinic,  $a = 16.916(1)$ ,  $b = 9.003(1)$ ,  $c = 17.688(1)$  Å,  $\beta = 93.83(1)^\circ$ ,  $V = 2687.85$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.28$  g cm<sup>-3</sup>,  $F(000) = 1104$ , Space group  $P2_1$  (No. 4), Cu- $K_\alpha$  radiation,  $\lambda = 1.54178$  Å,  $\mu(\text{Cu-}K_\alpha) = 7.9$  cm<sup>-1</sup>. A crystal of approximate dimensions 0.4 × 0.4 × 0.3 mm, recrystallised from aq. methanol, was mounted on an Enraf-Nonius CAD4 diffractometer and 25 reflections (with  $\theta$  ca. 30°) were used to determine accurate lattice parameters by least squares. Intensity data were collected for  $1^\circ < \theta < 76^\circ$ , using an  $\omega/2\theta$  scan, to yield a total of 5966 independent reflections measured, of which 4897 were considered observed with  $I > 3\sigma(I)$  and used in the subsequent refinement. The data were corrected for Lorentz and polarisation factors, but no absorption corrections were made. Crystallographic calculations were performed using the CRYSTALS system of programs.<sup>10</sup> The structure, [6-*O*-acetyl-9-*O*-[(*E*)-cinnamoyl]-1-*O*-glycoloyl-1,4,6,9-tetrahydroxy-dihydroagarofuran] (2), was solved by direct methods using the MULTAN program,<sup>11</sup> after several trial attempts, despite the

presence of two crystallographically independent molecules in the asymmetric unit which gave 74 non-hydrogen atoms to locate. Sixty-seven of these atoms were successfully located from the resulting *E*-map and the remaining atoms were located by Fourier methods. Full-matrix least-squares refinement, blocked into four half-molecule units to cater for the large number of parameters, and constrained to keep the sum of the *y*-coordinates fixed to define the origin in this direction, included anisotropic thermal parameters for non-hydrogen atoms and isotropic refinement of hydrogen atoms located in a difference Fourier synthesis terminated at *R* 0.0344 (*R*<sub>w</sub> 0.0446). A final difference map showed no features in excess of 0.2 e Å<sup>-3</sup>.

The refined fractional atomic co-ordinates are shown in Table 8. Thermal parameters, hydrogen atom positions, and significant Friedel pairs for vaalens-5 are all available on request from the Cambridge Crystallographic Data Centre.\*

The absolute configuration was investigated by inclusion of the small anomalous scattering of the oxygen atoms in the structure factor calculations.<sup>12</sup> The *R*-factor ratios (both weighted and unweighted) obtained for the two different inverted configurations were not found to differ significantly from unity.<sup>13</sup> However, these calculations were used to identify the most sensitive reflections to the absolute configuration, which showed the largest Bijvoet ratio. The reflections for which this ratio was greater than 10 were then remeasured, using a very long count time of 10 min, including the Friedel reflection pairs measured successively. The reflection pairs with a calculated theoretical Bijvoet ratio greater than 10, together with an observed intensity difference greater than 2 standard

Table 8. Fractional atomic co-ordinates for vaalens-5.

	Atom	<i>x</i>	<i>y</i>	<i>z</i>
Mol. (A)	C(1)	0.093 5(1)	0.917 5(3)	0.558 3(1)
	C(2)	0.054 3(2)	0.990 5(4)	0.488 4(2)
	C(3)	0.055 1(2)	0.880 4(4)	0.423 2(2)
	C(4)	0.138 3(1)	0.830 9(3)	0.405 5(1)
	C(5)	0.183 6(1)	0.769 7(3)	0.479 4(1)
	C(6)	0.270 9(1)	0.724 5(3)	0.474 3(1)
	C(7)	0.277 0(1)	0.603 0(3)	0.534 1(2)
	C(8)	0.281 5(2)	0.685 6(3)	0.610 6(2)
	C(9)	0.214 9(1)	0.796 8(3)	0.622 8(1)
	C(10)	0.180 2(1)	0.875 8(3)	0.549 7(1)
	C(11)	0.200 4(1)	0.514 0(3)	0.517 0(2)
	C(12)	0.172 3(2)	0.424 1(4)	0.582 5(2)
	C(13)	0.204 0(2)	0.408 0(3)	0.448 9(2)
	C(14)	0.182 0(2)	0.955 4(4)	0.365 6(2)
	C(15)	0.230 2(2)	1.018 3(3)	0.542 6(2)
	C(16)	0.035 2(2)	1.006 3(4)	0.668 8(2)
	C(17)	0.047 6(2)	1.103 3(5)	0.738 4(2)
	C(18)	0.344 2(2)	0.727 3(4)	0.363 5(2)
	C(19)	0.350 9(3)	0.650 4(7)	0.289 8(3)
	C(20)	0.150 6(2)	0.731 9(4)	0.735 6(2)
	C(21)	0.089 0(2)	0.634 0(4)	0.762 4(2)
	C(22)	0.076 3(2)	0.616 4(4)	0.834 2(2)
	C(23)	0.020 4(2)	0.513 0(4)	0.865 5(2)
	C(24)	-0.036 1(2)	0.435 9(5)	0.820 3(2)
	C(25)	-0.086 2(2)	0.334 4(5)	0.849 6(2)
	C(26)	-0.080 3(2)	0.305 2(5)	0.926 6(2)
	C(27)	-0.024 2(3)	0.378 4(5)	0.972 4(2)
	C(28)	0.025 5(2)	0.481 9(4)	0.942 6(2)
	O(1)	0.093 6(1)	1.018 3(2)	0.623 1(1)
	O(4)	0.130 4(1)	0.714 3(3)	0.350 5(1)
	O(5)	0.143 2(1)	0.633 1(2)	0.496 8(1)
	O(6)	0.286 9(1)	0.666 6(2)	0.400 8(1)
	O(9)	0.152 0(1)	0.721 1(2)	0.659 7(1)
	O(16)	-0.020 9(1)	0.927 0(4)	0.658 0(1)
	O(17)	0.100 5(2)	1.221 2(4)	0.732 9(2)
	O(18)	0.383 5(1)	0.830 5(4)	0.387 0(1)
	O(20)	0.194 4(2)	0.808 6(4)	0.774 5(1)

Table 8. (continued).

	Atom	<i>x</i>	<i>y</i>	<i>z</i>
Mol. (B)	C(51)	0.380 0(1)	0.350 0(3)	0.898 4(1)
	C(52)	0.451 0(2)	0.454 6(4)	0.945 3(2)
	C(53)	0.462 9(2)	0.389 9(4)	1.024 4(2)
	C(54)	0.385 8(2)	0.371 7(4)	1.064 2(1)
	C(55)	0.323 4(2)	0.282 7(3)	1.012 4(1)
	C(56)	0.239 0(2)	0.268 1(3)	1.038 5(1)
	C(57)	0.216 3(2)	0.117 0(4)	1.005 1(2)
	C(58)	0.198 1(2)	0.145 6(4)	0.919 5(2)
	C(59)	0.264 3(2)	0.222 3(3)	0.878 5(1)
	C(60)	0.314 6(1)	0.336 1(3)	0.927 7(1)
	C(61)	0.291 0(2)	0.024 2(3)	1.024 2(2)
	C(62)	0.300 7(3)	-0.111 2(4)	0.973 4(3)
	C(63)	0.299 7(3)	-0.029 1(5)	1.106 9(2)
	C(64)	0.357 5(3)	0.522 6(5)	1.091 1(2)
	C(65)	0.270 0(2)	0.485 9(4)	0.917 4(2)
	C(66)	0.442 5(2)	0.366 4(4)	0.773 7(2)
	C(67)	0.417 0(2)	0.416 8(5)	0.694 1(2)
	C(68)	0.177 4(2)	0.347 4(6)	1.148 4(2)
	C(69)	0.178 0(4)	0.328 2(9)	1.232 9(2)
	C(70)	0.316 4(2)	0.095 1(4)	0.772 8(1)
	C(71)	0.380 4(2)	-0.007 4(4)	0.754 2(2)
	C(72)	0.407 1(2)	-0.005 8(4)	0.685 1(2)
	C(73)	0.470 6(2)	-0.097 5(4)	0.657 7(2)
	C(74)	0.514 9(2)	-0.196 6(5)	0.704 0(2)
	C(75)	0.571 8(2)	-0.285 6(6)	0.675 1(2)
	C(76)	0.586 3(2)	-0.279 5(6)	0.599 4(2)
	C(77)	0.543 3(2)	-0.181 3(6)	0.552 9(2)
	C(78)	0.486 5(2)	-0.091 7(5)	0.581 4(2)
	O(51)	0.386 5(1)	0.400 5(2)	0.820 2(1)
	O(54)	0.404 0(2)	0.285 6(4)	1.130 9(1)
	O(55)	0.353 6(1)	0.131 5(2)	1.011 7(1)
	O(56)	0.234 9(1)	0.270 0(3)	1.1198 (1)
	O(59)	0.316 8(1)	0.112 0(2)	0.848 6(1)
	O(66)	0.503 1(1)	0.305 0(4)	0.792 0(1)
	O(67)	0.456 1(2)	0.345 4(4)	0.637 8(1)
	O(68)	0.133 8(2)	0.426 1(6)	1.111 2(2)
	O(70)	0.271 4(1)	0.157 1(3)	0.727 9(1)

deviations, were then analysed. Eight such reflection pairs were identified and of these 7 had their differences in the same sense, in accord with that shown on the formulae of this paper.

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\* See 'Instructions for Authors (1990),' *J. Chem. Soc., Perkin Trans. 1*, 1990.

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