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VULGARONE, A SESQUITERPENE KETONE WITH A NEW CARBON SKELETON FROM *CHRYSANTHEMUM VULGARE*

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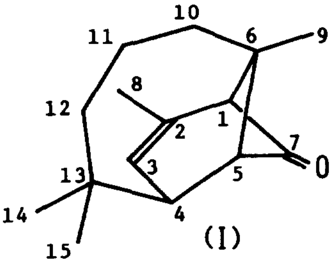
The essential oil of *Chrysanthemum vulgare* (L.) Bernhardi native in Europe has been investigated by many workers.1) From the plant, we have now isolated a novel sesquiterpene ketone named vulgarone, whose structure was determined to be formula I on the basis of spectroscopic comparison with chrysanthenone and preparation of the epoxide and LAH-reduction product. The present communication deals with the evidence for the proposed structure.

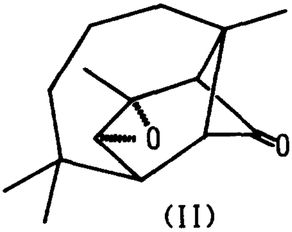
Vulgarone, $[\alpha]_D$ +113.7°(c 0.95, $CHCl_3$), was isolated in a homogeneous state, as examined by GLC and TLC, by eluting the steam volatile oil over a silica gel column with a mixed solvent of hexane and ethyl acetate together with (-)-chrysanthenone, $[\alpha]_D$ -55.2°(c 1.50, $CHCl_3$). The high resolution mass spectrum showed the molecular formula of the ketone to be $C_{15}H_{22}O$(M^+ obs. 218.1653, calc. 218.1669), and the ^{13}C-NMR, ^1H-NMR and IR spectra exhibited the presence of the following groups: a cyclobutanone($\nu_{max}^{CCl_4}$ 1780 cm^{-1}, δ_C 205.7 ppm),2) three tertiary methyls(gem-dimethyl, δ_C 26.1q, 30.4q, δ_H 0.93s, 1.01s; the other δ_C 27.7q, δ_H 1.18s), a trisubstituted double bond bearing a methyl group(δ_C 139.7s, 121.4d; δ_H 5.58m; δ_C 23.5q, δ_H 1.78t, J=2.0 Hz), three methylene(δ_C 42.2t, 33.2t, 21.5t, δ_H 1.25-1.65m) and three methines(δ_C 68.6d, 65.1d, δ_H 2.62dd, J=7.0, 1.0, δ_H 2.78ddd, J=7.0, 2.5, 1.5, AB type coupling; δ_C 55.6d, δ_H 2.38m). Although the ketone contained one more isoprene unit than chrysanthenone(IV), almost all of the functional groups were the same with those of the latter. Besides, the UV spectrum of the ketone showed an absorption band attributable to an β,γ-unsaturated carbonyl system3) at 292 nm(ε=88, EtOH) as well as that of chrysanthenone (295 nm, ε=144, EtOH).

Accordingly, the ketone was thought to have structural formula I, which reasonably explained the ^{13}C-NMR and ^1H-NMR spectra in comparison with those of chrysanthenone and its parent compound, α-pinene, as shown in Table I and II.

Irradiation of the vinylic proton at 5.58 reformed the triplet(1.78, of olefinic methyl), the double doublet(2.62) and double quartet(ddd, 2.78) of both α-methine protons in the cyclobutane residue, and a broad singlet(2.38, $W_{h/2}$ 7.0 Hz) of allylic proton into a doublet(J=2.0), doublet(J=7.0), double doublet(J=7.0, 2.5) and slightly narrow singlet($W_{h/2}$ 5.5 Hz) respectively; irradiation of



(I)



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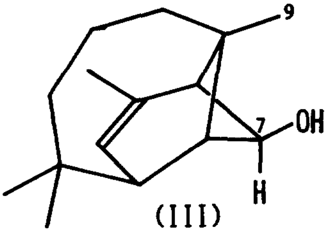

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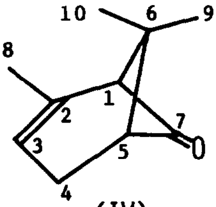

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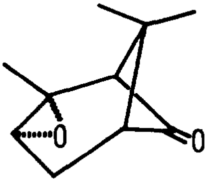

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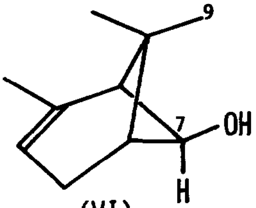

(VI)

the allylic proton at 2.38 caused the triplet(1.78) of the olefinic methyl to collapse to doublet(J=2.0). In addition, double irradiation of the olefinic methyl(1.78) and of the middle between the double doublet(2.62) and double quartet(ddd, 2.78) caused the multiplet(5.58) of the vinylic proton to become a doublet(J=2.5); double irradiation of the olefinic methyl(1.78) and allylic proton (2.38) reformed the multiplet(5.58) into a singlet($Wh_{1/2}$ 2.0) and that of the vinylic proton and the allylic proton reformed the triplet(1.78) into a singlet. The results of these decoupling experiments revealed that the molecule of the compound had cross-ring[4)] ($J_{1,5}$=7.0), allylic($J_{1,3}$=1.0 and $J_{3,8}$=2.0), vicinal ($J_{3,4}$=2.5 and $J_{4,5}$=1.5), homoallylic($J_{4,8}$=2.0) and M arrangement($J_{3,5}$=1.5) couplings, and such a coupling system had been reported in the molecule of cis-verbenol[5)] having the same configuration with α-pinene. Hence, it is certain that the ketone contains 3-methyl-bicyclo[3.1.1]heptan-1-one system as partial structure.

Next, the ^{13}C-NMR spectrum of the ketone is compared with those of chrysanthenone and α-pinene in Table I. The carbon atoms at 4- and 10-positions were characterized as a methine and methylene groups in this ketone, while they were present as the methylene and methyl groups in chrysanthenone and α-pinene. This fact indicated that the additional isoprene unit consisting of two methylene(δ_C 21.5, 42.2) and one gem-dimethyl(δ_C 26.1, 30.4) was inserted between 4-C and 10-C in the molecule of IV. Thus, the molecular structure of the ketone should be represented by formula I.

The further supports to the structure were obtained in preparation of the derivatives, epoxide and alcohol. Vulgarone was treated with m-ClPBA in CH_2Cl_2 to give a crystalline epoxide(II),[6)] $C_{15}H_{22}O_2$ (M^+ obs. 234.1613, calc. 234.1619); mp 105.5-106.5°; $[\alpha]_D$ -94.2°(c 0.52, $CHCl_3$); $\nu_{max}^{CCl_4}$ 3000, 1795, 1390, 1380, 1365,

Table I, Comparison of the ^{13}C-NMR[a]

Carbon atom	1	2	3	4	5	6	7	8
Vulgarone(I)	68.6(d)	139.7(s)	121.4(d)	55.6(d)	65.1(d)	37.1(s)	205.7(s)	23.5(q)
Chrysanthenone(IV)	67.9(d) (Δδ+20.7)[b]	138.7(s)	118.4(d)	33.0(t)	62.6(d) (Δδ+21.7)[b]	30.1(s)	205.8(s)	23.0(q)
α-Pinene	47.2(d)	144.4(s)	116.1(d)	31.5(t)	40.9(d)	38.1(s)	31.3(t)	20.9(q)

Carbon atom	9	10	11	12	13	14	15
Vulgarone(I)	27.7(q)	33.2(t)	21.5(t)	42.2(t)	35.2(s)	26.1(q)	30.4(q)
Chrysanthenone(IV)	27.3(q)	14.7(q)					
α-Pinene	26.5(q)	22.9(q)					

a) The spectra were taken in $CDCl_3$ on JEOL-FX60 spectrometer; Chemical shift(δc) are given in ppm relative to TMS.

b) $\Delta\delta=\delta_c^{ketone}-\delta_c^{hydrocarbon}$ in J.J. Burke and P.C. Lauterbur, J. Am. Chem. Soc., 86, 1876 (1964); J.B. Stothers, "Carbon-13 NMR spectrocsopy", Academic Press, New York, 1972, P177.

c) The assignment may be interchangeable.

Table II, Comparison of ^{1}H-NMR[d] and their aromatic solvent-induced shift 7)

	Vulgarone(I)						Chrysanthenone(IV)					
proton		CCl_4	C_6D_6	$\Delta\{\delta CCl_4-\delta C_6D_6\}$	C_6F_6	$\Delta\{\delta CCl_4-\delta C_6F_6\}$		CCl_4	C_6D_6	$\Delta\{\delta CCl_4-\delta C_6D_6\}$	C_6F_6	$\Delta\{\delta CCl_4-\delta C_6F_6\}$
1-H	dd	2.62	2.53	+0.09	2.54	+0.08						
3-H	m	5.58	5.43	+0.15	5.67	-0.09	m	5.30	5.00	+0.30	5.34	-0.04
4-H	m	2.38	2.31	+0.07	2.21	+0.17						
5-H	ddd	2.78	2.78	0.00	2.71	+0.07						
8-H	t	1.78	1.50	+0.28	1.80	-0.02	q	1.70	1.41	+0.29	1.73	-0.03
9-H	s	1.18	1.02	+0.16	1.19	-0.01	s	1.20	1.00	+0.20	1.22	-0.02
10-H 11-H 12-H	m	1.25~1.65	1.10~1.40		1.30~1.70		s	1.18	0.91	+0.27	1.28	-0.10
14-H[e]	s	0.93	0.69	+0.24	0.99	-0.06						
15-H[e]	s	1.01	0.82	+0.19	1.08	-0.07						

	Vulgarone epoxide(II)		Chrysanthenone 6) epoxide(V)		LAH reduction product(III)				cis-Chrysanthenol(VI) 8)			
proton		CCl_4		CCl_4		CCl_4	C_5D_5N	$\Delta\{\delta CCl_4-\delta C_5D_5N\}$		CCl_4	C_5D_5N	$\Delta\{\delta CCl_4-\delta C_5D_5N\}$
1-H	d	2.71	m	2.32	dd	1.92	2.18	-0.26				
3-H	brd	3.01	m	3.06	m	5.42	5.51	-0.09	m	5.13	5.18	-0.05
4-H	brd	2.08	m	2.32	m	2.08	2.18	-0.10				
5-H	ddd	2.52	m	2.69	ddd	2.26	2.52	-0.26				
7-H		-		-	s	3.80	4.19	-0.39	s	3.86	4.19	-0.33
8-H	s	1.44	s	1.38	t	1.70	1.69	+0.01	q	1.63	1.61	+0.02
9-H	s	1.18	s	1.13	s	1.50	1.86	-0.36	s	1.52	1.84	-0.32
10-H 11-H 12-H	m	1.40~1.90	s	1.30	m	1.10~1.70	1.20~1.80		s	0.88	0.98	-0.10
14-H[e]	s	1.11			s	0.96	0.96					
15-H[e]	s	0.99			s	0.93	0.91					

d) Chemical shift(δ_H) are given in ppm relative to TMS at 90 MHz.

e) These assignment may be interchanged.

845 cm^{-1}, and it was reduced with LAH in abs. Et$_2$O to afford an cis-alcohol(III), 6) $C_{15}H_{24}O$(M^+ obs. 220.1819, calc. 220.1825); mp 50.5-52.0°; $[\alpha]_D$ +45.9(c 1.80, $CHCl_3$); $\nu_{max}^{CCl_4}$ 3520, 3350, 3020, 1645, 1040 cm^{-1}. The ^{1}H-NMR spectra of both derivatives and solvent shift of III, showed good correspondence toward those of chrysanthenone epoxide(V) and chrysanthenol(VI) even in 3-H and 8-H(epoxy methine) of II and 7-H(secondary hydroxyl methine) and 9-H(hydroxyl side methyl) of III as seen Table II.

Lastly, the ORD curve was taken in order to determine the absolute configuration, a strong positive cotton effect($[\phi]_{307}$ +6490, $[\phi]_{291}$ 0, $[\phi]_{273}$ -3680, a=101.7, in isooctane) which was just as (+)-chrysanthenone(IV)($[\phi]_{311}$ +9000, $[\phi]_{296}$ 0, $[\phi]_{276}$ -8030, a=170.3, in isooctane) 3) being recognized. Accordingly, the absolute configuration of vulgarone should be represented by formula I, whose chirality is the same with that of IV with regard to the β,γ-unsaturated keto chromophore.

Biogenetically, vulgarone may be synthesized via the stereospecific cyclization of α-cis-bergamotene.

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