Journal of Natural Products
Vol. 51, No. 3, pp. 588-590, May-Jun 1988

ISO-ALOERESIN A, A MINOR CONSTITUENT OF CAPE ALOE[1]

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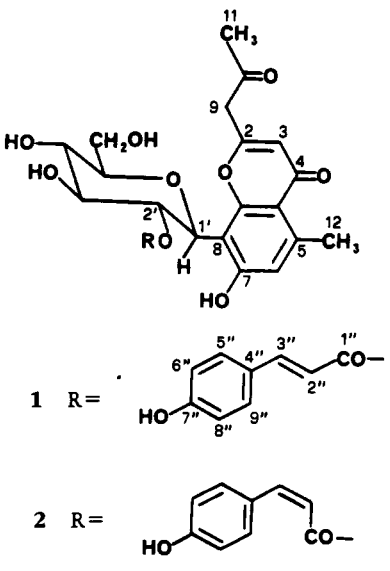
Aloe is the solid residue obtained by the concentration of the resinous exudate from the cut leaves of *Aloe ferox* Mill. (Liliaceae) and its hydrids (Cape and Kenya aloe) and *Aloe vera* L. (synonym, *Aloe barbadensis* Mill.) (Curaçao aloe) (2). Previous investigations showed that the drug is particularly rich in 5-methylchromone *C*-glucosides, i.e., aloeresin A [**1**] (3), aloesin (formerly aloeresin B) (4), aloeresin C (5), and aloeresin D (6). As a part of our chemical investigations on minor constituents of aloe, we wish to report here the isolation of a new 5-methylchromone component of Cape aloe, which we have named iso-aloeresin A. Its structure was shown to be 2-acetonyl-8-*C*-β-D-[2-*O*-(*Z*)-*p*-coumaroyl]-glucopyranosyl-7-hydroxy-5-methylchromone [**2**] on the basis of chemical and spectral evidence.

When an MeOH/H_2O extract of Cape aloe was examined by analytical hplc, it was shown to contain a still unidentified component with an Rt just lower than that of the most abundant aloeresin A [**1**]. The new compound was isolated by preparative hplc as a white amorphous solid in ca. 0.9% yield from the starting drug. Its uv and ir spectra revealed strong resemblances with those of *C*-glucosylated 5-methylchromones (5,6), and the fabms spectrum exhibited ions at *m/z* 563 $[M+Na]^+$ and 541 $[M+H]^+$, like those of aloeresin A [**1**].



1 R=

2 R=

The isomeric relationship between **1** and the compound under investigation (iso-aloeresin A) was proved by inspection of their ^1H- and ^{13}C-nmr spectra. The major differences in the ^1H-nmr spectra (Table 1) of the two isomers appeared in the chemical shifts and coupling constants of the protons at C-2″ and C-3″ of the *p*-coumaroyl group. The observation that methyl (*E*)- and (*Z*)-*p*-coumarates differ similarly allowed the structure **2** to be assigned to iso-aloeresin A.

The structure **2** for iso-aloeresin A was confirmed conclusively by chemical correlation. On irradiation of an aqueous solution of aloeresin A [**1**] with a white fluorescent lamp, a photostationary state was reached, corresponding to a mixture of **1** and a more polar compound in a ratio ca. 60:40 (estimated by hplc). The photochemically formed compound, when isolated in the usual manner, was found to be identical in all respects (fabms, uv, ir, ^1H and ^{13}C nmr) with iso-aloeresin A obtained from Cape aloe.

It must be pointed out that the proton resonance frequencies of the *p*-coumaroyl group occur in the aloeresins **1** and **2** at significantly higher fields than they do in the corresponding *E* and *Z* methyl es-

[1]Part 5 in the series "Studies on Aloe." For part 4, see G. Speranza *et al.* (1).

TABLE 1. ^{1}H-nmr Spectral Data for Compounds **1** and **2** and for Methyl *p*-Coumarate Isomers (DMSO-d_6, after D_2O exchange).[a]

Proton(s)	**1**[b,c]	Methyl (*E*)-*p*-coumarate	**2**[b]	Methyl (*Z*)-*p*-coumarate
H-3	6.18 (s)		6.16 (s)	
H-6	6.61 (s)		6.59 (s)	
-CH_2CO-	3.81 (s)		3.77 (s)	
MeCO-	2.29 (s)		2.24 (s)	
MeAr	2.60 (s)		2.61 (s)	
H-1′	4.93 (d, 9.0)		4.87 (d, 9.8)	
H-2′	5.51 (dd, 9.0)		5.46 (dd, 9.8)	
H-2″	6.16 (d, 15.0)	6.39 (d, 16.0)	5.52 (d, 12.6)	5.78 (d, 12.8)
H-3″	7.34 (d, 15.0)	7.57 (d, 16.0)	6.62 (d, 12.6)	6.87 (d, 12.8)
H-5″, H-9″	7.48 (d, 8.5)	7.55 (d, 8.5)	6.95 (d, 8.6)	7.65 (d, 8.7)
H-6″, H-8″	6.77 (d, 8.5)	6.80 (d, 8.5)	6.52 (d, 8.6)	6.77 (d, 8.7)
MeO-		3.69 (s)		3.65 (s)

[a]Chemical shifts (multiplicity; *J*, Hz).
[b]The remaining sugar protons (H-3′ to H-6′) gave complex overlapping signals in the region 3.0–4.0 δ.
[c]See Speranza *et al.* (5).

ters as shown in Table 1. The aromatic protons H-5″ and H-9″ of the *cis*-coumaroyl residue have suffered more upfield shift.

Taking into account that 8-*C*-glucosylflavones exist in two main rotational conformers (7), the plane of the pyranosyl ring being approximately perpendicular to the chromone nucleus, it is reasonable to assume that the same conformations occur in aloeresins. An inspection of molecular models reveals that the 2′-*O*-substituent is situated above or below the plane of the chromone nucleus, thus undergoing a shielding effect. Such an effect was reported for the signal of the 2″-*O*-acetyl group of various acetylated 8-*C*-glucosylflavones (8). The fact that the upfield shift is exceptionally pronounced in the case of the 5″,9″ protons of iso-aloeresin A [**2**] is accounted for by the assumed conformations in which the two equivalent protons are located close to and in front of the aromatic chromone ring.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Hplc was carried out on Partisil ODS-3 (Whatman) columns 10 μm, 250 × 4 mm (analytical) or 250 × 20 mm (preparative) using either MeOH/H_2O linear gradient from 30 to 60% MeOH in 25 min (eluent A) or MeOH/H_2O linear gradient from 20 to 60% MeOH in 40 min (eluent B), flow rate of 1 ml/min and 15 ml/min for analytical and preparative separations, respectively, and uv detection at λ 280 nm in both cases. ^{1}H-nmr (300 MHz) and ^{13}C-nmr (75.47 MHz) spectra were recorded on a Bruker CXP 300 spectrometer in DMSO-d_6, using the solvent signal as internal reference (2.50 and 39.50 ppm from TMS for ^{1}H and ^{13}C, respectively). Fabms spectra were taken on a VG 707 EQ mass spectrometer. All compounds were protected from light during their isolation and purification.

PLANT MATERIAL.—Commercial Cape aloe used in this investigation was purchased from Pan-African Corporation (Cape Town, South Africa). It was the same specimen used in previous studies (5). A voucher specimen is on deposit in the Centro Studi M. Branca, Milan.

ISOLATION OF ISO-ALOERESIN A [**2**].—Powdered Cape aloe (1.0 g) was dissolved in 100 ml of hot MeOH. After filtration of insoluble material, the extract was passed through a C_{18} PrepSep cartridge (Allied Fisher Scientific). The eluate was concentrated in vacuo to give a brown residue that was subjected to preparative hplc (eluent A). Fractions containing iso-aloeresin A as a major product (Rt 13.0 min) were combined and further purified by preparative hplc (eluent B, Rt 32.2 min). After lyophilization, compound **2** was obtained as an amorphous powder (7.3 mg). It was shown to be pure by analytical hplc (eluent A, Rt 12.2 min). Mp 134–136°; $[\alpha]^{30}D$ +139.6° (*c* = 0.25, MeOH); ir ν max (KBr) 1725, 1655, 1605, 1510, 1465, 1385 cm^{-1}; uv λ max (MeOH) 224 (log ε 4.61), 242 sh (4.44), 250 (4.43), 296 nm (4.50); ^{1}H nmr see Table 1; ^{13}C nmr (DMSO-d_6) δ 202.3 (C-10), 178.5 (C-4), 164.9 (C-1″), 160.3 (C-2 or C-7), 159.4 (C-7 or C-2), 158.5 (C-1a, C-7″), 142.7 (C-3″), 140.9 (C-5), 132.0 (C-5″, C-9″), 124.9 (C-4″), 115.7 (C-6), 115.0 (C-2″), 114.6 (C-6″, C-8″, C-4a), 112.5 (C-3), 109.0 (C-8), 81.9 (C-5′), 75.7 (C-3′), 72.0 (C-2′), 70.6 (C-1′, C-4′), 61.7 (C-6′), 48.0 (C-9), 29.6 (C-11), 22.7 (C-12);

fabms *m/z* 563 $[M+Na]^+$, 541 $[M+H]^+$. Calcd for $C_{28}H_{28}O_{11}\cdot H_2O$: C 60.21, H 5.41%; found C 60.35, H 5.35%.

ISOMERIZATION OF ALOERESIN A [**1**].—Aloeresin A [**1**] (250 mg) (5) was dissolved in 50 ml 45% EtOH. After deoxygenation by N_2 bubbling, the solution was irradiated with a 20-W fluorescent lamp (OSRAM L 20 W). Irradiation was performed at room temperature using a cylindrical (Pyrex glass) reactor surrounded by a copper jacket with a sealed coil for circulating cold H_2O (10°). The progress of isomerization was followed by analytical hplc (eluent A) of aliquots taken at 15-min intervals. After 4 h the reaction mixture was found to contain aloeresin A (Rt 13.3 min) and a more polar compound (Rt 12.2 min) in the ratio 6:4, which remained constant with further exposure to light. The solution was then concentrated, and the residue was separated by preparative hplc (eluent B) to give starting aloeresin A and a compound (70 mg) which was found to have identical physical and chromatographic properties to natural iso-aloeresin A [**2**].

PREPARATION OF METHYL (*E*)-*p*-COUMARATE.—*p*-Coumaric acid (1.0 g) was refluxed in MeOH (100 ml) containing HCl (1%) for 4 h. Usual work-up and crystallization from MeOH afforded pure methyl (*E*)-*p*-coumarate in 90% yield. Mp 136–137° [lit. (9) mp 136–137°]; ^{1}H nmr see Table 1; ^{13}C nmr (DMSO-d_6) δ 167.1 (C-1″), 159.9 (C-7″), 144.8 (C-3″), 130.3 (C-5″, C-9″), 125.1 (C-4″), 115.8 (C-6″, C-8″), 113.9 (C-2″), 51.2 (OCH_3).

PREPARATION OF METHYL (*Z*)-*p*-COUMARATE.—Methyl (*E*)-*p*-coumarate (100 mg), dissolved in 45% EtOH (100 ml), was irradiated as described above for aloeresin A. The progress of isomerization was monitored by analytical hplc (eluent A, Rt 16.5 and 18.5 min for *Z* and *E* methyl esters, respectively). After 25 h (isomeric ratio 57:43 and favor of the *E* isomer) the solvent was removed and the residue separated by preparative hplc (eluent A) to give the title compound in 32% yield. Mp 87° [lit. (10) mp 85.5–86°]; ^{1}H nmr see Table 1; ^{13}C nmr (DMSO-d_6) δ 166.5 (C-1″), 158.9 (C-7″), 143.4 (C-3″), 132.5 (C-5″, C-9″), 125.4 (C-4″), 115.1 (C-2″), 114.9 (C-6″, C-8″), 51.1 (OCH_3).

ACKNOWLEDGMENTS

We gratefully acknowledge Dr. D. Monti, Centro di Studio per le Sostanze Organiche Naturali del CNR, University of Milan, for running nmr spectra, Centro Studi M. Branca, Milan, and the Ministero Pubblica Istruzione of Italy for financial support.

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Received 28 September 1987