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ALOECHRYSONE, A DIHYDROANTHRACENONE FROM *ALOE BERHANA*

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Key Word Index—*Aloe berhana*; Asphodelaceae; roots; leaves; dihydroanthracenones; (*R*)-aloechrysone; anthraquinones.

Abstract—Analysis of the roots of *Aloe berhana* resulted in the isolation of aloesaponol I, laccaic acid D methyl ester, aloesaponol III, aloesaponarin I, chrysophanol-8-methyl ether, chrysophanol, and the new dihydroanthracenone 3,4-dihydro-3,9-dihydroxy-8-methoxy-3-methyl-1(2*H*)-anthracenone named aloechrysone.

INTRODUCTION

The genus *Aloe* comprises over 360 species distributed mainly in Tropical and Southern Africa, Madagascar and Southern Arabia [1]. Reynolds [2] recorded some 37 species of *Aloe* in Ethiopia. Although the leaves of many *Aloe* species have been investigated for their chemical constituents, phytochemical studies of the roots are limited to only a few reports by Yagi and coworkers [3–6].

Aloe berhana is an endemic species growing on roadsides near the town of Debre Berhan, central Ethiopia. From the roots of this plant, we have isolated and characterized the new pre-anthraquinone **1**, for which the trivial name aloechrysone is suggested. In addition, we report here the isolation of the known compounds: chrysophanol-8-methyl ether (**2**), aloesaponol I (**3**), laccaic acid D methyl ester, aloesaponol III, aloesaponarin I and chrysophanol.

RESULTS AND DISCUSSION

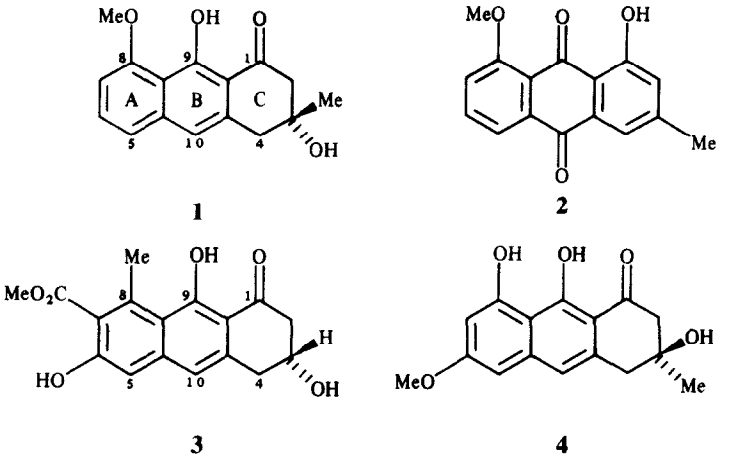
TLC of the acetone extract of the roots of *A. berhana* revealed the presence of at least nine spots, one of which (R_f 0.25, solvent system 2) showed greenish fluorescence when viewed at 366 nm. Separation of this pale-yellow compound, aloechrysone (**1**), was achieved by means of CC over silica gel followed by preparative TLC and purification over Sephadex LH-20.

Aloechrysone (**1**) was optically active ($[\alpha]_D$ −25° (MeOH)). The molecular formula $C_{16}H_{16}O_4$ followed from the HR mass spectrum. The UV-VIS spectrum, by virtue of its similarity to that of torosachrysone (**4**), suggested the presence of a dihydroanthracenone chromophore. A low field singlet at δ15.95 in the ^{1}H NMR spectrum indicated the presence of a chelated hydroxyl group at C-9. The aromatic region portrayed an ABC pattern at δ6.81 (*br d*), 7.20 (*br d*) and 7.48 (*t*) suggesting that ring A is only substituted at C-8. The H-10 resonance appeared at δ6.99 as a broad singlet. The three-proton singlets at δ3.95 and 1.45 indicated a methoxyl and a methyl group, respectively. Placement of the methoxyl at C-8 was confirmed by an NOE experiment, in which irradiation of the resonance at δ3.95 resulted in enhancement of the signal due to H-7 (δ6.81). The C-2 and C-4 methylene proton resonances appeared in chloroform-*d* as broad singlets at δ2.85 and 3.10, respectively, whereas in acetone-d_6 they gave rise to a pair of AB quartets. Similar observations were made by Gill *et al.* [7] for structurally related dihydroanthracenones.

The ^{13}C NMR and 2D ^{1}H–^{13}C COSY spectra of aloechrysone are in full accord with structure **1**. Thus, the ^{13}C NMR spectrum reveals the presence of a carbonyl (δ202.7), two methylene groups (δ43.5 and 51.9), a methoxyl (δ56.1), a methyl (δ28.7), four aromatic methine groups, one aliphatic and six aromatic quaternary carbons. In the 2D ^{1}H–^{13}C COSY spectrum, the carbon resonance at δ117.9 correlates with the proton resonance at δ6.99 (H-10) and the resonance at δ105.8 with the doublet at δ6.81 (H-7), in full agreement with structure **1**. Thus, aloechrysone is 3,4-dihydro-3,9-dihydroxy-8-methoxy-3-methyl-1(2*H*)-anthracenone (**1**).

Treatment of **1** with 10% NaOH resulted in its conversion to chrysophanol-8-methyl ether (**2**). This derivative proved to be identical to a compound also present in the acetone extract of the roots. Demethylation of **2** with HBr gave rise to chrysophanol. The occurrence of **2** in *Cassia* species (Leguminosae) and *Ventilago calyculata* (Rhamnaceae) has been reported before [8], but this constitutes the first report of this compound in an *Aloe* species.

We assign the (*R*)-configuration to **1** on comparison of its CD spectrum (Fig. 1) with that of (*S*)-torosachrysone (**4**) [7, 9]. It should be noted that the absolute configuration of torosachrysone isolated from *Cassia singuena* was established as *S* by exciton chirality experiments involving the 3-*O*-benzoyl derivative of torosachrysone-8,9-di-*O*-methyl ether [10] and by chemical correlation with (−)-quinic acid [9]. Likewise the absolute configuration of aloesaponol I (**3**) was determined by Yagi *et al.* [4] to be (*R*) by application of the extended benzoate chirality rule. Aloesaponol I obtained from *A. berhana* must have the (*R*)-configuration as it gave rise to a CD curve with the same signs as that observed for (*R*)-aloechrysone (Fig. 1). It is interesting to speculate on the chemotaxonomic or other significance of the difference in configuration at C-3 of dihydroanthracenones obtained from *Aloe* and *Cassia* species.



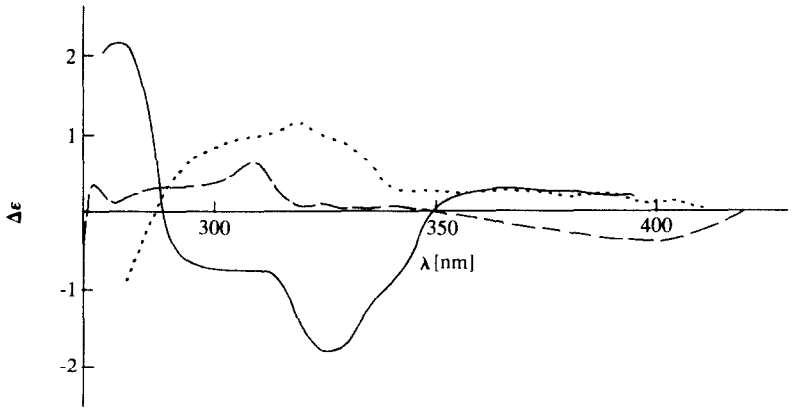


Fig. 1. The CD spectra of (*R*)-aloechrysone (– – –), (*S*)-torosachrysone (——) and (*R*)-aloesaponol I (- - - - -).

Atrochrysone and its 6-*O*-methyl ether, torosachrysone (**4**), play a significant role in the biogenesis of anthraquinone and pre-anthraquinone pigments in fungi [11] and can be considered as progenitors of emodin and physcion, respectively. The isolation and characterization, in this study, of (*R*)-aloechrysone (**1**) indicates the likely presence in nature of a precursor of the common anthraquinone chrysophanol.

EXPERIMENTAL

General. ^{1}H and ^{13}C NMR: 400 and 100 MHz, respectively, or 90 and 22.5 MHz in $CDCl_3$ or Me_2CO-d_6; UV: MeOH; IR: KBr discs; MS: 70 eV, direct inlet system; mps: uncorr; TLC: Kieselgel 60 F_{254} layers (0.2 mm) using $CHCl_3$–EtOAc (1:1, solvent system 1), C_6H_6–EtOAc (4:1, solvent system 2), C_6H_6 (solvent system 3), C_6H_6–EtOAc (9:1, solvent system 4).

Plant material. Roots of *Aloe berhana* Reynolds were collected from 120 km north of Addis Ababa on the Debre Berhan road. The plant was identified by Dr Sebsebe Demissew, National Herbarium, Addis Ababa University, where a voucher specimen under the cipher Sebsebe 2209 is kept.

Extraction and isolation. Dried and powdered roots of *A. berhana* (500 g) were extracted with Me_2CO at ambient temp. for 5 days. Evapn of the Me_2CO yielded 9.0 g crude extract, which was subjected to VLC (thin layer grade silica gel; petrol–EtOAc mixtures of increasing polarities). Fourteen 100 ml frs were collected. Frs 1–3 (10% EtOAc) gave chrysophanol (6 mg); frs 4–6 (20% EtOAc) contained a mixture which was separated by prep. TLC (solvent system 2) to give chrysophanol-8-methyl ether (**2**, 4 mg) and aloesaponarin I (12 mg). From frs 7–8 (30% EtOAc) aloesaponol III (6 mg) pptd out. Frs 9–12 (30% EtOAc) proved to be a mixture which was separated by prep. TLC (solvent system 2) followed by purification using Sephadex LH-20 (MeOH) to yield aloechrysone (**1**, 7 mg) and laccaic acid D methyl ester (7 mg). From frs 13–14 (100% EtOAc) aloesaponol I (10 mg) pptd out.

(R)-*Aloechrysone* (**1**). R_f 0.25 (solvent system 2); mp 161–163° (Me_2CO); $[\alpha]_D$ −25° (MeOH; *c* 0.1); UV λ_{max} nm: 229, 252, 292, 306, 392; IR ν_{max} cm^{-1}: 3480, 2950, 1625, 1580, 1460, 1400, 1380, 1280, 1090; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (3H, *s*, Me), 2.85 (2H, *s*, H-2), 3.10 (2H, *s*, H-4), 3.95 (3H, *s*, OMe), 6.99 (1H, *br s*, H-10), 6.81 (1H, *d*, J = 8 Hz, H-7), 7.20 (1H, *d*, J = 8 Hz, H-5), 7.48 (1H, *t*, J = 8 Hz, H-6), 15.05 (1H, *s*, OH-9); ^{13}C NMR (100 MHz, $CDCl_3$): δ202.7 (C-1), 165.7 (C-8), 159.8 (C-9), 142.7 (C-10a), 140.2 (C-4a), 135.5 (C-6), 119.7 (C-5), 117.9 (C-10), 115.5 (C-8a), 110.6 (C-9a), 105.8 (C-7), 70.8 (C-3), 56.1 (OMe), 51.9 (C-4), 43.5 (C-2), 28.7 (C-Me); HR-EIMS *m/z* (rel. int.): 272.1062 $[M]^+$ (100) ($C_{16}H_{16}O_4$ requires 272.1048), 239 (23), 215 (20), 214 (45), 196 (20), 192 (35).

Conversion of (R)-*aloechrysone* (**1**) *to chrysophanol-8-methyl ether* (**2**). Compound **1** (2 mg) was stirred in 10% aq. NaOH (4 ml) overnight. This was then acidified and extracted with $CHCl_3$ to yield **2**, identical (EIMS, ^{1}H NMR, co-TLC) in all respects with chrysophanol-8-methyl ether isolated from *A. berhana*.

(R)-*Aloesaponol I* (**3**). R_f 0.25 (solvent system 1); mp 238–240° (plates from MeOH) (lit. [3] 248–250°); UV λ_{max} nm: 278, 318, 381; IR ν_{max} cm^{-1}: 3360, 3150, 1720, 1620, 1600, 1480, 1440; ^{1}H NMR (DMSO-d_6): δ15.26 (1H, *s*, OH-9); (CD_3OD): δ2.78 (1H, *ddd*, J = 17, 7.1 Hz, H-2a), 2.81 (3H, *s*, Me), 3.02 (2H, *m*, H-2e and H-4a), 3.24 (1H, *dd*, J = 16, 3.5 Hz, H-4e), 4.38 (1H, *tt*, J = 7, 3.5 Hz, H-3), 6.88 (1H, *s*, H-5), 6.92 (1H, *s*, H-10); ^{13}C NMR (100 MHz, CD_3OD): δ204.7 (C-1), 171.1 (C-12), 167.9 (C-6), 156.7 (C-9), 142.9 (C-4a), 139.0 (C-10a), 138.0 (C-8), 126.7 (C-9a), 118.0 (C-10), 117.5 (C-7), 111.6 (C-8a), 108.6 (C-5), 66.7 (C-3), 52.8 (OMe), 48.5 (C-4), 38.9 (C-2), 21.2 (C-Me); HR-EIMS *m/z* (rel. int.): 316.0946 $[M]^+$ (20) ($C_{17}H_{16}O_6$ requires 316.0947), 284 (100), 266 (19), 256 (28), 228 (18), 210 (20).

Aloesaponol III. R_f 0.28 (solvent system 2); mp 186–188° (Me_2CO) (lit. [4] 198–200°); UV λ_{max} nm: 224, 246, 256, 270; IR ν_{max} cm^{-1}: 3550, 3400, 2950, 1640, 1610, 1580, 1380; ^{1}H NMR: identical to that reported in ref. [4]; MS *m/z* (rel. int.): 258 $[M^+]$ (100), 240 (54), 225 (17), 201 (17); treatment of this compound first with acid and then with base as described in ref. [4] led to its conversion to chrysophanol.

Aloesaponarin I. R_f 0.50 (solvent system 2); mp 190–192° (EtOH) (lit. [3] 199–203°); UV, IR, MS and ^{1}H NMR: identical to that reported [3].

Laccaic acid D methyl ester. R_f 0.45 (solvent system 1); mp 282–284° (Me_2CO) (lit. [3] 270–275°); found $[M]^+$ 328.0593, $C_{17}H_{12}O_7$ requires 328.0583; UV, IR, ^{1}H NMR, MS: identical to those reported [3].

Chrysophanol. Identical with authentic sample (co-TLC); R_f 0.60 (solvent system 3); mp 194–196° (EtOH) (lit. [12] 196°).

Chrysophanol-8-methyl ether (**2**). R_f 0.65 (solvent system 3); mp 198–200° (MeOH) (lit. [8] 197°); found $[M]^+$ 268.0732, $C_{16}H_{12}O_4$ requires 268.0736; UV, IR, ^{1}H NMR: identical to that reported [8]; EIMS *m/z* (rel. int.): 268 $[M]^+$ (100), 250 (46), 222 (57).

Conversion of compound **2** *to chrysophanol*. To compound **2** (1 mg) dissolved in $CHCl_3$ was added 5 drops of HBr (48%) and the mixture stirred for 30 min. H_2O was then added and the $CHCl_3$ layer sepd. Removal of the solvent yielded chrysophanol (co-TLC).

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