

THE MOLECULAR STRUCTURE AND ABSOLUTE CONFIGURATION OF BRACHYCARPONE, A NEW TRINORTRITERPENOID DILACTONE FROM *CLEOME BRACHYCARPA*

VIQAR UDDIN AHMAD,* KHISAL AHMAD ALVI,

H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-32, Pakistan

and MASOOD A. KHAN*

National Research Council, Atlantic Research Laboratory,

1411 Oxford Street, Halifax, N.S. B3H 3Z1, Canada

ABSTRACT.—A new trinortriterpenoid, brachycarpone (**1**), has been isolated from *Cleome brachycarpa*. The molecular structure and the absolute configuration of **1** are established from the spectroscopic and X-ray crystallographic studies.

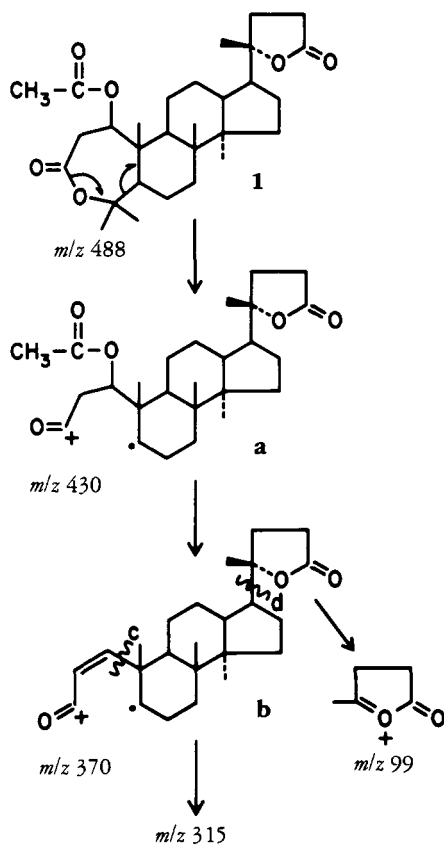
Cleome brachycarpa Vahl ex DC. (Capparidaceae) grows widely in Pakistan (**1**) and is reported to be useful for the treatment of scabies, rheumatism, and inflammation (**2**). No work on the chemical constituents of this plant has been reported so far. In this paper, we wish to report the isolation, spectroscopic studies, and X-ray analysis of a new trinortriterpenoid obtained from the alcoholic extract of *C. brachycarpa* and now named brachycarpone (**1**).

RESULTS AND DISCUSSION

Brachycarpone (**1**), mp 228°, analyzed for C₂₉H₄₄O₆. The uv spectrum of **1** shows only end absorption at 208 nm, and the ir spectrum (KBr) shows peaks at 1765 (γ lactone), 1720, and 1730 (ester and 7-membered lactone). The ¹H-nmr (100 MHz) spectrum of **1** in CDCl₃ shows the presence of six quaternary methyl groups as singlets at δ 0.89 (3H), 1.02 (3H), 1.09 (3H), 1.35 (3H), and 1.49 (6H). The relative downfield positions of the last two peaks are consistent with quaternary methyl groups attached to an oxygen-bearing carbon. A sharp peak at δ 2.09 (3H) is assigned to an acetate methyl, and there is a double doublet at δ 4.84 (*J*=6.1, 2.1 Hz) due to the proton attached to carbon bearing the acetoxy group (**3**). In addition, a multiplet at δ 3.10 (2H) is assigned to methylene protons adjacent to the carbonyl group of the 7-membered lactone (**3**), and another multiplet centered at δ 2.54 could be assigned to the two methylene groups which are α and β to the carbonyl group of the γ-lactone ring (**4**).

The mass spectrum of brachycarpone does not show the molecular ion peak at *m/z* 488. The highest peak at *m/z* 430 (**a**) (Scheme 1) is formed through the elimination of a molecule of Me₂CO from the molecular ion. Other important peaks in the spectrum are at *m/z* 370 (**b**, **a** minus HOAc), 315 and 99 (base peak, C₅H₇O₂). The ¹³C-nmr spectrum shows the presence of two lactone carbonyl peaks at δ 169.55 and 176.4 ppm and an acetoxy group (δ 170.48 and 20.58 ppm). The ¹³C-nmr assignments were made on the basis of an attached proton test (APT) experiment and comparison with the chemical shifts of compounds of similar structure (**3**).

An X-ray crystallographic study of a single crystal was performed to establish the structure and the absolute configuration of **1**. A computer generated diagram of **1**, in the correct absolute configuration, is presented in Figure 1. Compound **1** has a 7-membered lactone ring with the acetoxy group at C-1. The ring fusions A-B, B-C, and C-D are *trans*. Individual rings A, B, and C adopt slightly deformed chair conformations, while the 5-membered ring D adopts a half-chair conformation. Bond lengths and angles are normal, except for the bonds involving (C23) [C(22)-C(23), 1.431 (7) and C(23)-C(24), 1.477 (7)]. These unusually short bonds are presumably caused by the



slight disorder of C(23) atomic position with the disorder of the C(23) atom reflected in the unusually high thermal parameter of this atom.

The absolute configuration of **1** was determined by carefully measuring 16 Friedel pairs that were most sensitive to the anomalous dispersion effect of CuK α radiation. Fifteen pairs indicated the absolute configuration shown in Figure 1, and only one pair showed no consistent absolute configuration. In order to check for any systematic errors, these measurements were repeated with MoK α radiation. The anomalous disper-

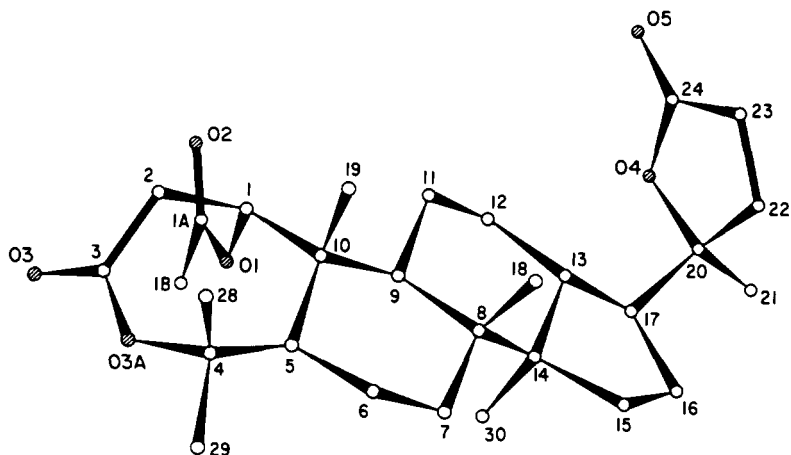


FIGURE 1. Structure of **1** with the atomic labeling. Hydrogen atoms are omitted for clarity.

sion effect of MoK α radiation would be insignificant; therefore, the intensity difference of I⁺ and I⁻ should vanish. This proved to be correct. Hence, the absolute configuration of **1** was established unequivocally. The enantiomer shown in Figure 1 has the (2*S*) stereochemistry which is similar to that reported for methyl shoreate (5), cabraleone (6), and the related bromo-compound (7).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded in KBr discs with a Jasco A-302 spectrometer and the ¹H- and ¹³C-nmr spectra on 100 and AM-100 spectrometers. Mass spectra were recorded on a Finnigan MAT 312 mass spectrometer fitted with a direct inlet system.

The plant material of *C. brachycarpa* was collected in Karachi, Pakistan, in August 1984, and identified by the Department of Botany, University of Karachi. A voucher specimen has been deposited in the herbarium of the Department of Botany, University of Karachi.

EXTRACTION AND ISOLATION.—The plant material (30 kg) was cut into small pieces and finely divided in an Ultra-Turrex homogenizer under 95% EtOH. The extract was filtered and concentrated under reduced pressure to a gum. The latter was partitioned between H₂O and hexane.

The hexane layer was evaporated, and 30 g of the residue was chromatographed on a column of silica gel (400 g) (E. Merck, Cat. No. 10180). Elution was carried out with solvent gradient of increasing polar-

TABLE 1. Atomic Parameters for **1** (e.s.d.s. refer to the last digit printed)

ATOM	x	y	z	Beq. ^a
O1	0.5628(2)	-0.6527(1)	0.3515(1)	4.8
O2	0.7143(3)	-0.7009(1)	0.2528(2)	9.9
O3	0.3473(2)	-0.7714(1)	0.3421(3)	6.9
O3A	0.2391(2)	-0.6811(1)	0.3776(2)	5.9
O4	1.0463(2)	-0.3958(1)	0.3047(2)	5.8
O5	1.1040(3)	-0.4152(2)	0.1475(2)	10.1
C1	0.4898(3)	-0.6275(2)	0.2647(2)	4.5
C1A	0.6725(4)	-0.6896(2)	0.3346(3)	6.6
C1B	0.7305(5)	-0.7126(3)	0.4308(3)	10.3
C2	0.3925(4)	-0.6821(2)	0.2329(2)	5.5
C3	0.3257(3)	-0.7144(2)	0.3206(2)	5.4
C4	0.1991(3)	-0.6108(2)	0.3689(3)	5.6
C5	0.3225(3)	-0.5653(2)	0.3790(2)	4.8
C6	0.2782(3)	-0.4951(2)	0.4094(2)	5.4
C7	0.3941(4)	-0.4561(1)	0.4533(2)	5.4
C8	0.5131(3)	-0.4479(1)	0.3801(2)	4.7
C9	0.5485(3)	-0.5167(1)	0.3360(2)	4.3
C10	0.4291(3)	-0.5597(1)	0.2931(2)	4.5
C11	0.6707(4)	-0.5120(2)	0.2656(2)	5.3
C12	0.7942(3)	-0.4840(2)	0.3171(2)	5.5
C13	0.7605(3)	-0.4178(1)	0.3649(2)	4.7
C14	0.6412(3)	-0.4229(2)	0.4372(2)	4.8
C15	0.6378(4)	-0.3524(2)	0.4792(3)	6.1
C16	0.7860(4)	-0.3333(2)	0.4929(3)	6.7
C17	0.8689(4)	-0.3816(2)	0.4254(2)	5.5
C18	0.4695(2)	-0.3978(2)	0.2987(3)	5.9
C19	0.3746(4)	-0.5312(2)	0.1923(2)	5.7
C20	0.9800(3)	-0.3464(1)	0.3673(3)	5.5
C21	1.0873(4)	-0.3207(2)	0.4382(3)	7.2
C22	0.9342(4)	-0.2937(2)	0.2925(3)	7.2
C23	0.9818(6)	-0.3157(3)	0.1967(4)	13.1
C24	1.0512(4)	-0.3795(2)	0.2083(3)	7.3
C28	0.1089(4)	-0.6014(2)	0.2766(3)	7.2
C29	0.1100(4)	-0.6061(2)	0.4626(3)	7.1
C30	0.6760(4)	-0.4682(2)	0.5278(2)	6.7

^aBeq = 8 π^2 [$\frac{1}{3}$ (U₁₁ + U₂₂ + U₃₃)]

ity. The fraction eluted with hexane-EtOAc (6:4) was recrystallized from Et₂O to yield brachycarpone (**1**) (200 mg) mp 228°; [α]_D +25.6° (c 1, CHCl₃); found C, 71.22, H, 8.77 calcd for C₂₉H₄₄O₆, C, 71.28, H, 9.08%; ir (KBr) 1762m 1730, 1720 cm⁻¹; ¹H nmr 0.89 (s, 3H), 1.02 (s, 3H), 1.09 (s, 3H), 1.35 (s, 3H), 1.49 (s, 6H), 2.09 (s, OCOCH₃), 2.54 (m), 3.10 (m, 2H), 4.84 (dd, *J*=6.1, 2.1 Hz); ¹³C nmr C-1 (71.27), C-2 (42.84), C-3 (169.55), C-4 (86.00), C-5 (42.84), C-6 (21.63), C-7 (30.94), C-8 (41.75), C-9 (51.16), C-10 (40.05), C-11 (21.04), C-12 (24.83), C-13 (44.07), C-14 (50.46), C-15 (31.46), C-16 (24.83), C-17 (49.23), C-18 (15.90), C-19 (15.48), C-20 (89.55), C-21 (24.88), C-22 (28.95), C-23 (30.94), C-24 (176.42), C-28 (23.65), C-29 (24.88), C-30 (15.41), OCOCH₃ (170.48), OCOCH₃ (20.58); ms *m/z* (rel. int.) M⁺ absent, 430 (10), 370 (50), 315 (20), 195 (20), 99 (100).

CRYSTALLOGRAPHY.—Preliminary unit cell dimensions were determined from photographic data, and more accurate values from the least-squares analysis of the diffractometer, setting of 24 high angle (104-127°) reflections (radiation=CuK α , λ =1.54056Å).

Crystal Data. ¹—C₂₉H₄₄O₆, mw 488.67, cell dimensions at T=23° are: a=9.976 (2) Å, b=20.329 (2) Å, c=13.288 (1) Å, orthorhombic space group P2₁2₁2₁, Z=4, ρ_{calc} =1.205 g/cm³, ρ_{exp} =1.20 g/cm³.

A crystal of approximate dimensions of 0.2 x 0.2 x 0.4 mm was mounted along the longest dimension, and the data were collected on a Picker 4-circle diffractometer, using Ni-filtered CuK α radiation. The θ -2 θ , scan method was used, and individual reflection profiles were analyzed as described by Grant and Gabe (8). Three standard reflections, monitored after every 60 measurements, showed no significant intensity changes during data collection.

The standard deviations were evaluated from the counting statistics; reflections with $I_{\text{net}} \geq (2\sigma(I_{\text{net}}))$ were classed as 'observed' and were used in the subsequent analysis. These numbered 1784 of a possible 2640 ($2\theta_{\text{max}} = 130^\circ$). Lorentz and polarization corrections were applied to the intensities.

The structure was solved by direct methods using MULTAN 80 (9) and refined by block-diagonal least-squares method. Positional and anisotropic thermal parameters were refined for all the nonhydrogen atoms. Positional parameters and individual isotropic temperature factors were refined only for the methyl hydrogen atoms, while all the other hydrogen atoms were included in the idealized position (C-H=1.08Å). Convergence was achieved with the final R-value=0.037 and R_w=0.047. Final difference map was featureless with the largest peak being 0.1 e Å⁻³.

The computer programs used for calculations have been described by Larson and Gabe (10). The atomic scattering factors were taken from International Tables, Vol. IV (11). Final atomic coordinates are listed in Table 1.

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¹Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Center and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, U.K.