Journal of Natural Products
Vol. 51, No. 2, pp. 360-363, Mar-Apr 1988

THE CRYSTAL STRUCTURE OF SCOPADULCIC ACID A FROM PARAGUAYAN CRUDE DRUG "TYPYCHÁ KURATÛ" (*SCOPARIA DULCIS*)

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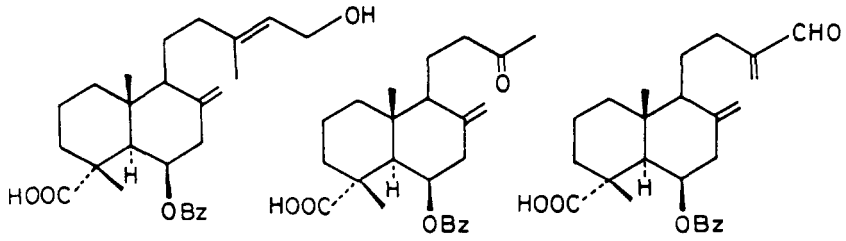
In our search for biologically active substances in Paraguayan medicinal plants, we have isolated five cytotoxic diterpenoids named scoparic acids A [**1**], B [**2**], and C [**3**], and scopadulcic acids A [**4**] and B [**5**] from whole plants of *Scoparia dulcis* L. (Scrophulariaceae). They were characterized as new diterpenoids on the basis of spectral data including 2D-nmr spectra (1–3). Among them, scopadulcic acids A [**4**] and B [**5**] were found to have a novel skeleton. Scopadulcic acid A [**4**] was obtained as colorless prisms, and its structure has now been confirmed by single crystal X-ray analysis. The crystal structure of scopadulcic acid A is illustrated in Figure 1.

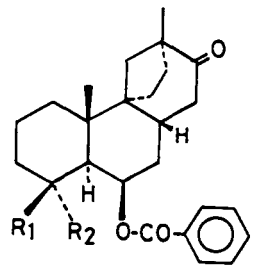
EXPERIMENTAL

PLANT MATERIAL.—Whole plants of *S. dulcis* were collected near Asuncion, Paraguay, in April 1986. The voucher specimens are deposited in the Herbal Garden of the Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, and Sección Botanica, Facultad de Ciencias Químicas, Universidad Nacional de Asunción.

EXTRACTION AND ISOLATION OF SCOPADULCIC ACID A.—The whole parts of air-dried *S. dulcis* were ground to a fine powder and



1 Bz=COC_6H_5 **2** Bz=COC_6H_5 **3** Bz=COC_6H_5



4 R_1=COOH, R_2=CH_2OH
5 R_1=Me, R_2=COOH

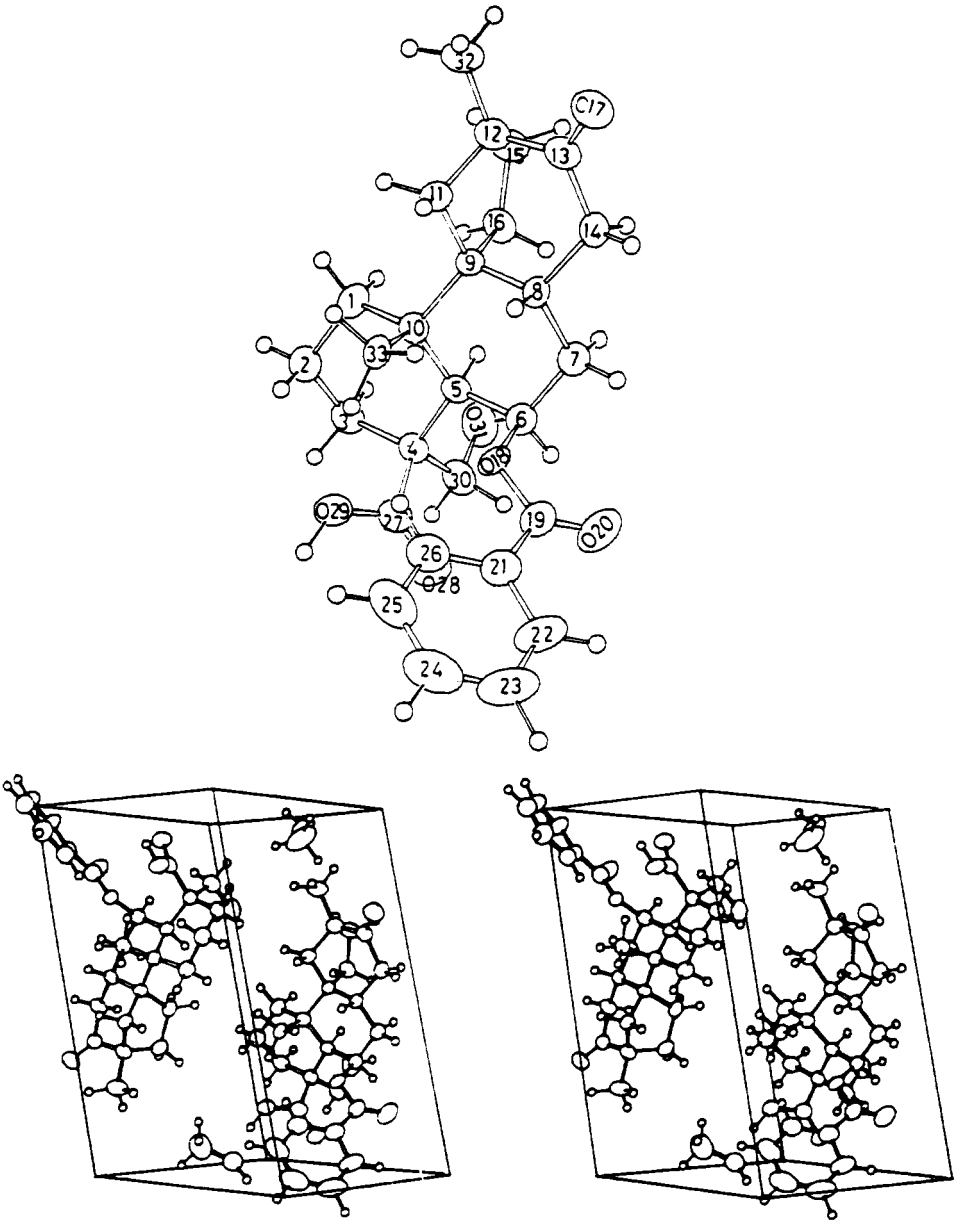


FIGURE 1. Crystal structure of scopadulcic acid A [**4**] and its molecular packing.

extracted with 70% EtOH at boiling temperature (1 h, 3 times). The extract (333 g) was suspended in H_2O and extracted with *n*-hexane. The part that was insoluble in both solvents (67.1 g) was filtered off and was further extracted with $CHCl_3$. The $CHCl_3$-soluble part (54.3 g) was repeatedly chromatographed on a Si gel column ($CHCl_3$/MeOH and *n*-hexane/EtOAc) to afford 130 mg of scopadulcic acid A [**4**].

SCOPADULCIC ACID A [**4**].—$C_{27}H_{34}O_6$, mp 172–174° (MeOH), $[\alpha]_D$ −5.7° (MeOH), ^{13}C nmr (100.4 MHz, Me_2CO-d_6) δ 35.1 (C-1), 20.1 (C-2), 33.5 (C-3), 48.8 (C-4), 45.0 (C-5), 70.4 (C-6), 35.8 (C-7), 37.0 (C-8), 54.2 (C-9), 40.0 (C-10), 46.5 (C-11), 53.2 (C-12), 212.8 (C-13), 43.5 (C-14), 37.7 (C-15), 24.6 (C-16), 20.5 (C-32), 68.2 (C-30), 178.3 (C-27), 21.6 (C-33), 166.8 (C-19), 132.5 (C-21), 130.8 (C-22, C-26), 129.5 (C-23, C-25), 133.7 (C-24).

CRYSTALLOGRAPHIC ANALYSIS OF **4**.—Scopadulcic acid A [**4**] was analyzed as its MeOH solvate. A crystal of dimensions 0.5 × 0.5 × 0.2 mm was selected for X-ray measurements. Crystal data: $C_{27}H_{34}O_6$·MeOH, M_w 486.6, mono-

TABLE 1. Fractional Atomic Coordinates ($\times 10^4$) and Temperature Factors ($Å^2 \times 10^3$) for Non-hydrogen Atoms of Scopadulcic Acid A [**4**].

Atom	x	y	z	U_{eq}
C-1	5512(5)	2990	5041(7)	45(2)
C-2	6372(5)	3130(9)	6364(7)	46(2)
C-3	7097(5)	2000(9)	6309(7)	40(2)
C-4	7458(5)	1940(7)	4872(7)	32(2)
C-5	6629(5)	2170(7)	3474(7)	31(2)
C-6	6971(5)	2271(7)	2030(8)	35(2)
C-7	6155(5)	2147(8)	677(7)	36(2)
C-8	5311(4)	3072(7)	731(7)	30(2)
C-9	4957(4)	2943(7)	2178(7)	28(2)
C-10	5825(5)	3231(8)	3561(7)	33(2)
C-11	4116(5)	3952(8)	2081(7)	35(2)
C-12	3286(5)	3291(8)	956(8)	40(2)
C-13	3526(5)	3378(7)	−558(8)	35(2)
C-14	4489(5)	2789(9)	−631(7)	40(2)
C-15	3378(5)	1758(9)	1491(9)	46(3)
C-16	4455(5)	1502(8)	2198(8)	38(2)
O-17	2994(4)	3872(7)	−1626(6)	50(2)
O-18	7469(3)	3589(5)	2034(5)	35(2)
C-19	8164(5)	3625(9)	1262(8)	44(2)
O-20	8302(4)	2690(7)	493(7)	75(2)
C-21	8720(5)	4912(9)	1502(8)	44(2)
C-22	9480(6)	5056(11)	815(11)	68(3)
C-23	10041(6)	6191(13)	1026(11)	82(4)
C-24	9845(6)	7238(12)	1919(11)	70(4)
C-25	9100(7)	7130(11)	2604(10)	66(3)
C-26	8536(5)	5964(9)	2399(9)	49(3)
C-27	8313(5)	2919(9)	4963(7)	40(2)
O-28	9012(3)	2646(6)	4497(6)	52(2)
O-29	8231(3)	4131(6)	5614(6)	48(2)
C-30	7886(5)	490(9)	4803(8)	45(3)
O-31	7191(4)	−563(6)	4717(6)	55(2)
C-32	2316(5)	3935(10)	942(9)	56(3)
C-33	6129(5)	4754(7)	3540(7)	33(2)
O-34	373(4)	889(7)	3717(7)	68(2)
C-35	781(9)	1916(15)	3061(14)	111(6)

clinic, space group $P2_1$, a = 14.355(2), b = 9.732(2), c = 9.297(2) Å, β = 103.30(1)°, V = 1263.9(4) Å^3, Z = 2, D_x = 1.28 Mg·m^{-3}, μ(MoKα) = 0.977 cm^{-1}. Data were collected by a Rigaku AFC-5 diffractometer equipped with graphite monochromated MoKα radiation (λ = 0.7107 Å) and 2θ-ω scan mode. Unit cell parameters were determined by least-squares fit of 47 strong reflections (29° ≦ 2θ ≦ 37°). Of the 2521 reflections measured (3° ≦ 2θ ≦ 50°), 2367 were unique and 1786 with Fo ≧ 2σ(Fo) were considered observed and used in the calculations. The crystal structure was solved by direct methods using MULTAN 78 (4) and refined by full-matrix least-squares on F using unit weight (5). The positions of H atoms were calculated from an idealized geometry and checked with the D maps. Convergence was achieved with R = 0.063. For the fractional atomic coordinates and the temperature factors for non-hydrogen atoms of **4** see Table 1.[1]

ACKNOWLEDGMENTS

We are grateful to Dr. Kazuhide Kamiya and Mr. Yoshikazu Wada of Central Research Division, Takeda Chemical Industries, Ltd. for X-ray measurement and helpful discussions.

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

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Received 25 September 1987