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SCOPADULCIC ACID-A AND -B, NEW DITERPENOIDS WITH A NOVEL SKELETON, FROM A PARAGUAYAN CRUDE DRUG "TYPYCHÁ KURATÜ" (SCOPARIA DULCIS L.)

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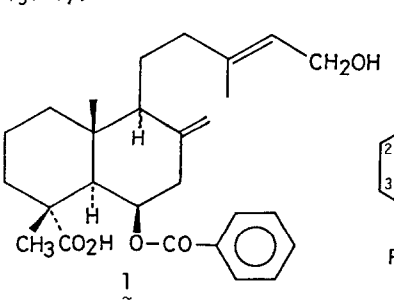
Abstract: Scopadulcic acid-A and -B, diterpenoids with a novel skeleton, have been isolated from the whole plants of Scoparia dulcis L., and their structures, including the absolute configuration, were determined based on the 2-D NMR and CD spectral data.

During our investigation on biologically active substances from Paraguayan medicinal plants, a new labdane-type diterpenoid, scoparic acid-A (1), was isolated from the 70% ethanol extract of "Typychá kuratü" (whole plants of Scoparia dulcis L., Scrophuraliaceae).[1] From the same source, we have now isolated two novel diterpenoids, named scopadulcic acid-A (2) and -B (3). In this communication, structures of scopadulcic acid-A and -B, including their absolute stereochemistry, are described.

Scopadulcic acid-A (2), colorless prisms (MeOH), mp 172-174°, $[\alpha]_D^{27}$-5.7° (MeOH), has the molecular formula $C_{27}H_{34}O_6$ (M^+ 454.2313, calcd. 454.2354) and its UV and IR spectra showed absorption maxima at 229 (log ε:4.15), 275sh (2.98), 277 (3.02) and 280 (2.94) nm and at 3500 (OH), 1710, 1700 (CO), 1600, 1590 (phenyl) cm^{-1}, respectively. The ^1H- and ^{13}C-NMR spectra of 2 indicated the presence of two carbonyls (δ_C 178.2 and 212.8), a benzoyl (δ_H 7.43, 7.57, 7.96; δ_C 129.5, 130.8, 132.5, 133.7 and 166.8), a hydroxymethylene (δ_H 3.56 and 3.79, each d, J=10.6 Hz; δ_C 68.2) and two tert-methyl groups (δ_H 1.01 and 1.60; δ_C 20.5 and 21.6) and four quarternary sp^3 carbons (δ_C 40.0, 48.8, 53.2 and 54.2). These data coupled with the detailed analyses of the ^1H-^1H and ^1H-^{13}C COSY spectra[2] suggested that 2 has the partial structures A and B (Fig. 1).



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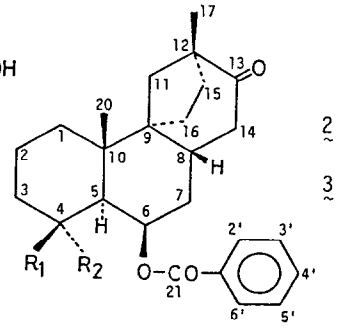

2: R_1= COOH, R_2= CH_2OH

3: R_1= CH_3, R_2= COOH

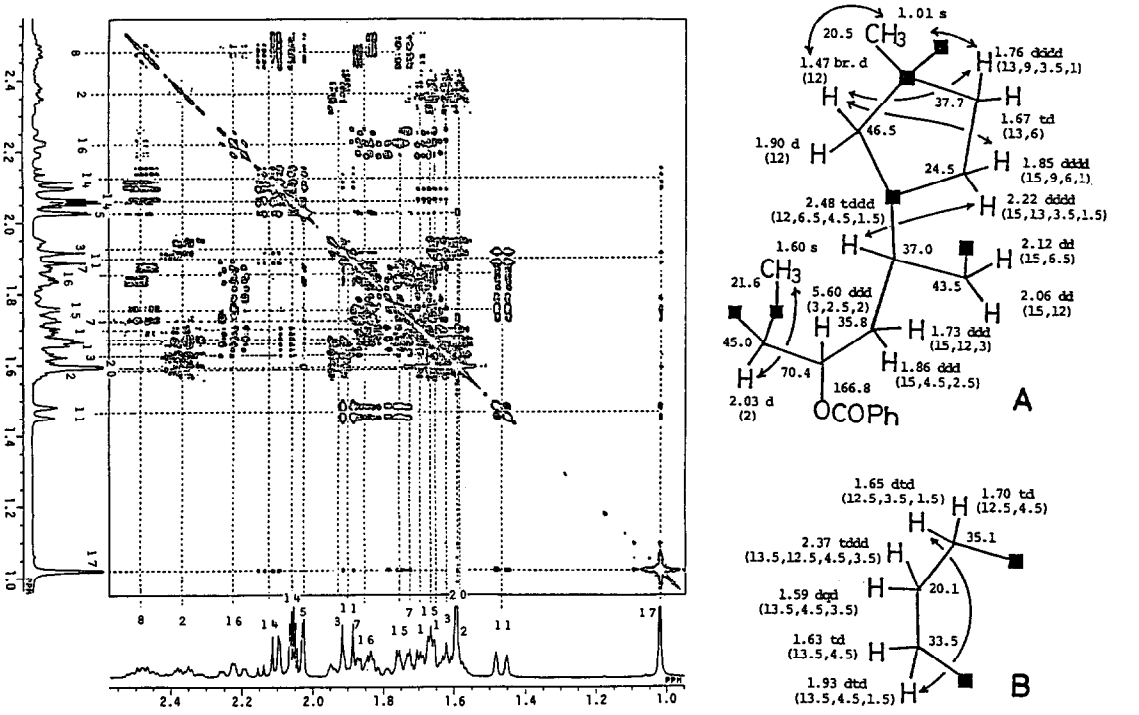

Fig. 1 Highly Resolved ^{1}H-^{1}H COSY Spectrum of Scopadulcic acid-A (2) in the High Field Region (in Acetone-d_6) and Partial Structures in 2 (⇝ : long-range coupling observed; coupling constants in parenthesis)

Then, we measured the ^{1}H-^{13}C long-range COSY spectrum of 2 in order to clarify the connectivities of the partial structures and substituent groups. As shown in Fig. 2, the carbon signal at δ45.0 (C-5) is connected with the proton signals at δ1.70 (1-H), 1.93 (3-H), 1.86 (7-H), 3.79 (18-H) and 1.60 (20-H_3) in terms of long-range correlation, while the quarternary carbon signal at δ48.8 (C-4) with the protons at δ1.93 (3-H) and 2.03 (5-H). Also, the quarternary carbon signals at δ54.2 (C-9), 40.0 (C-10) and 53.2 (C-12) are correlated with the proton signals at δ1.86 (7-H), 1.90 (11-H), 2.06 (14-H), 2.22 (16-H) and 1.60 (20-H_3), at δ1.65 (1-H), 2.03 (5-H), 5.60 (6-H) and 1.60 (20-H_3), and at δ1.90 (11-H) and 1.01 (17-H_3), respectively. Thus, the planar structure of scopadulcic acid-A was assigned to the formula 2a in Fig. 2, in which some of other significant long-range correlations observed are also shown by arrows.

The relative stereochemistry was elucidated on the basis of the coupling constants of each proton and the results of NOE experiments. Irradiation of the 20-methyl and the 8-proton caused the increase of the signal intensity of the 11-, 20-, and 2',6'-protons and the 8-, 11-, and 2', 6'-protons, respectively. Also, NOE's between the 5- and 6-protons and between the 5- and 16-protons were observed. These findings enabled us to determine the stereostructure of scopadulcic acid-A to be 2b as depicted in Fig. 3.

Scopadulcic acid-B (3), colorless prisms (MeOH), mp 228-232°, $[\alpha]_D^{27}$ -49.6° (MeOH), has the molecular formula $C_{27}H_{34}O_5$ (M^+ 438.2420, calcd. 438.2415) and it showed the UV and IR spectra very similar to those of 2. Extensive studies of the ^{1}H- and ^{13}C-NMR spectra of 3[3] compared with those of 2 indicated that both are closely related compounds with each other, but 3 has an

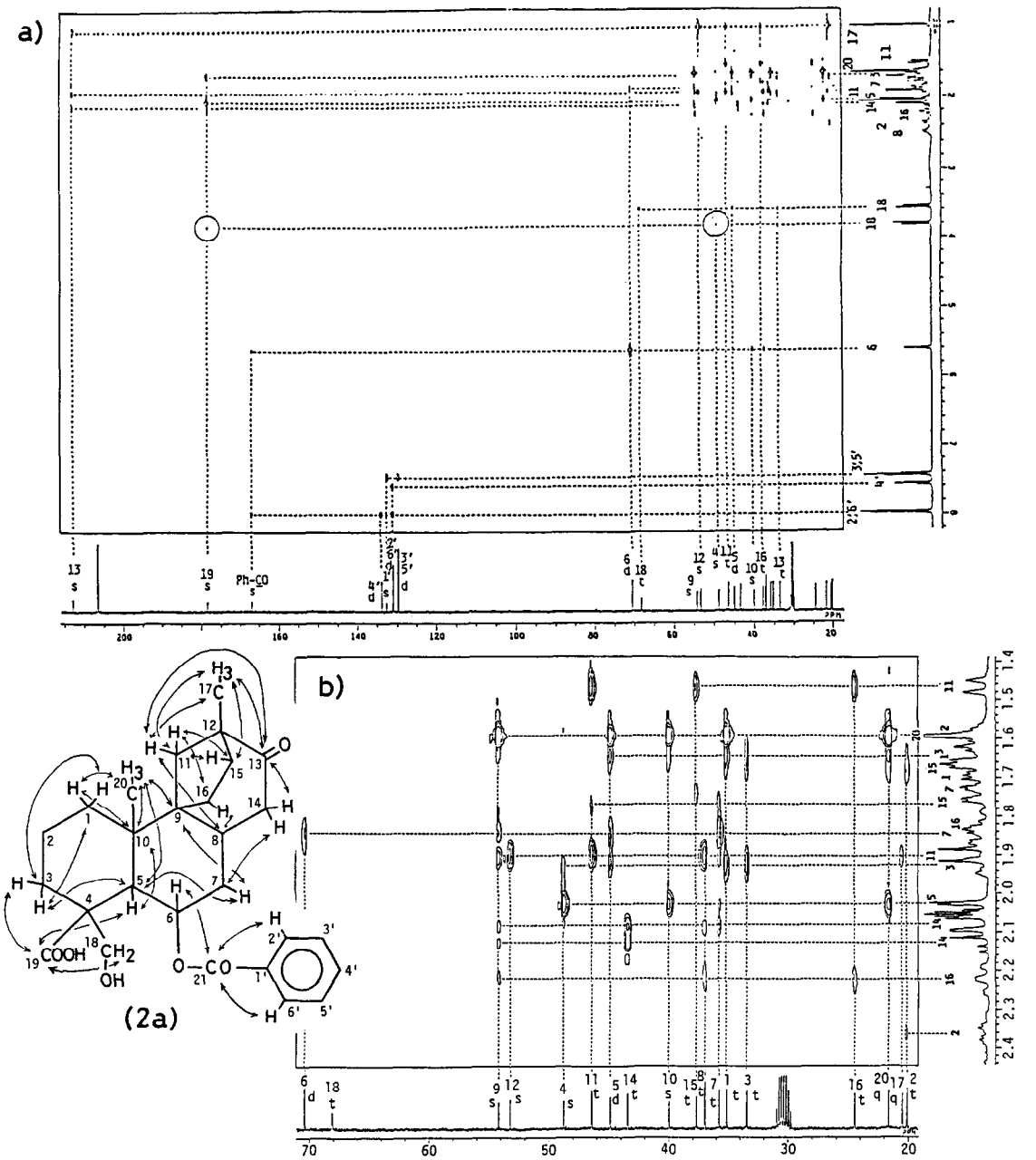

Fig. 2 ^{1}H-^{13}C Long-range COSY Spectrum of Scopadulcic acid-A (2) in Acetone-d_6
a) Whole Region, b) High Field Region (Sample: 20 mg, 20°C, J_{CH}=10 Hz, 12 hr run)
Multiplicities of carbon signals were determined by the off-resonance and DEPT methods and are indicated as s, d, t and q. Open circles indicate the correlation peaks, which are significant but weak at this threshold level.

additional tert-methyl group instead of the hydroxymethylene group in 2. Further, NOE's were observed as shown in the formula 3a (Fig. 3). Thus, the structure of scopadulcic acid-B was assigned to the formula 3.

The absolute configuration of scopadulcic acid-A and -B was determined as 2 and 3,

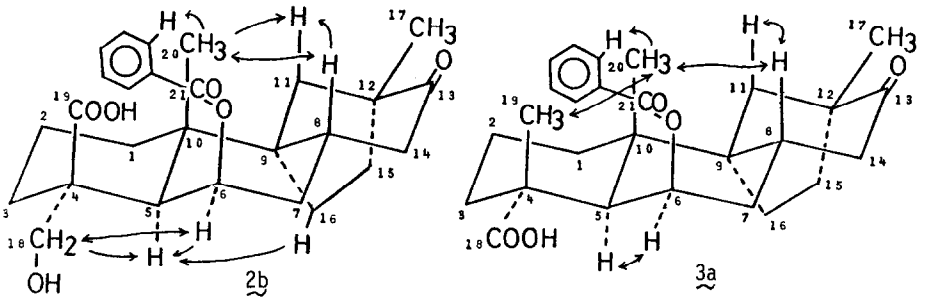

Fig. 3 NOE's Observed in Scopadulcic acid-A and -B

respectively, based on the fact that both compounds showed the positive Cotton effect due to the optically active ketone chromophore in the CD spectra (CD maximum: 2, $[\theta]_{297}^{MeOH}$ +2130; 3, $[\theta]_{297}^{CHCl_3}$ +2490). Octant projection of the structures (2b and 3a) reasonably supports these assignments.

It should be noted that scopadulcic acid-A (2) and -B (3) represent a new class of diterpenoids and particularly, they are of interest from a biogenetic view-point.[4] The biological activities of these compounds are now under examination.

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References and Notes

1) M. Kawasaki, T. Hayashi, M. Arisawa, M. Shimizu, S. Horie, H. Ueno, H. Shogawa, S. Wada, Y. Namose, S. Suzuki, M. Yoshizaki, N. Morita, Y. Tezuka, T. Kikuchi, L.H. Berganza, E. Ferro and I. Basualdo, the 107th Annual Meeting of the Pharmaceutical Society of Japan, Kyoto, April, 1987, p. 326.

2) A. Bax, "Two-Dimensional NMR in Liquids", D. Reidel Publishing Co., Dordrecht, Holland, 1982; R. Benn and H. Gunther, Angew. Chem. Int. Ed. Engl., 22, 350 (1983).

3) ^{1}H-NMR of 3 ($CDCl_3$,δ): 1-H_2 (1.75 and 1.62), 2-H_2 (1.61 and 1.79), 3-H_2 (1.63 and 1.82), 5-H (2.22, d, J=2 Hz), 6-H (5.33, td, J=3, 2 Hz), 7-H_2 (1.76, ddd, J=15, 12, 3 Hz and 1.88, ddd, J=15, 4.5, 3 Hz), 8-H (2.49, tdd, J=12, 6.5, 4.5 Hz), 11-H_2 (1.54, br.d, J=12.5 Hz and 1.83, d, J=12.5 Hz), 14-H_2 (2.02, dd, J=16, 12 Hz and 2.25, dd, J=16, 6.5 Hz), 15-H_2 (1.62 and 1.81), 16-H_2 (1.86 and 2.21), 17-H_3 (1.10, s), 19-H_3 (1.36, s), 20-H_3 (1.56, s), 2',6'-H_2 (8.02, d, J=7.3 Hz), 3',5'-H_2 (7.45, t, J=7.3 Hz), 4'-H (7.57, t, J=7.3 Hz).
^{13}C-NMR of 3 ($CDCl_3$,δ): 213.6 (13-C), 184.2 (18-C), 166.1 (21-C), 133.4 (4'-C), 130.5 (1'-C), 129.6 (2',6'-C), 128.5 (3',5'-C), 72.9 (6-C), 53.1 (9-C), 52.3 (15-C), 47.2 (4-C), 45.1 (11-C), 44.6 (5-C), 42.5 (14-C), 39.7 (3-C), 38.8 (10-C), 36.6 (16-C), 36.0 (8-C), 35.1 (7-C), 34.0 (1-C), 23.7 (16-C), 21.6 (20-C), 19.7 (17-C), 19.3 (19-C), 18.0 (2-C).

4) A diterpenoid with similar skeleton has recently been reported, see F. Bohlmann, C. Zdero, R. M. King and H. Robinson, Liebigs Ann. Chem., 1984, 250.

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