Tetrahedron Letters No.57, pp. 6007-6010, 1968. Pergamon Press. Printed in Great Britain.

A NEW BITTER PRINCIPLE FROM BRUCEA SUMATRANA ROXB.[1]

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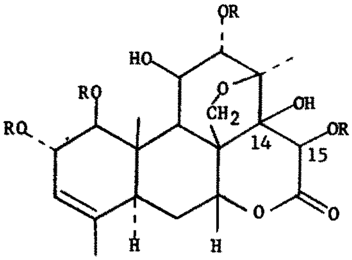
(Received in USA 16 October 1968; received in UK for publication 24 October 1968)

In continuing our systematic study of the bitter principles of plants of the family Simaroubaceae (2), we have investigated the non-lipophilic material from the seeds of Brucea sumatrana Roxb. and have isolated a new lactone. This compound is described here by the number WST-63, for while its properties are in good accord with those reported from yatanoside, a compound earlier isolated from the same plant (3), those of its acetyl derivative and the acetate of yatanoside differ (4).

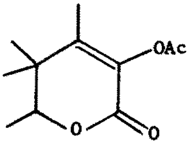
WST-63, $C_{20}H_{28}O_9$, m.p. 258-258.5°, $[\alpha]_D$ + 21.1 (c 0.4, pyridine), gives a purple color with concentrated H_2SO_4, a behavior characteristic of a number of compounds of the Simaroubaceae (5). It is different from brusatol (2) and from the bruceines A, B, C (6) and G (7). Acetylation of WST-63 under mild conditions (pyridine-acetic anhydride, 25°, one week) gave a crystalline tetraacetate, $C_{28}H_{36}O_{13}$, m.p. 255-256.5°, $[\alpha]_D$ + 42.3° (c 0.50, pyridine), which still showed hydroxyl absorption (IR, $CHCl_3$, 3570 cm^{-1}) and which was not oxidized with CrO_3 (pyridine) under mild conditions.

The n.m.r. spectrum (Table I) of the tetraacetate was in accord with the structures I (for WST-63) and II (for the tetraacetate). Of special importance are the n.m.r. signals

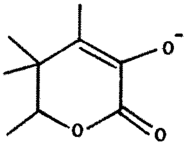


I, R = H

II, R = Ac



III



IV

at δ 6.12 (singlet, 1-H), δ 3.25 (s, 1-H), and δ 2.72 (doublet, 1-H, J = 7 Hz). The latter two signals disappeared after addition of D_2O and are assigned to a tertiary and a secondary hydroxyl group, respectively. The singlet at δ 6.12 is assigned to the proton at C-15. Its appearance suggested that the tertiary hydroxyl group was located at the adjacent C-14, a supposition that was confirmed as follows.

Treatment of the tetraacetate with $SOCl_2$ in pyridine gave the anhydro-tetraacetate (partial structure III), $C_{28}H_{34}O_{12}$, m.p. 245-246°, in which the secondary hydroxyl group is still present (doublet, 1-H, at δ 2.69, disappearing with addded D_2O), whose ultraviolet spectrum showed only an increased absorption near 200 nm (ε about 14000) compared with the original tetraacetate. After addition of a drop of 1 N KOH solution a new maximum slowly appeared at 291.5 nm, which is characteristic of the partial structure IV (8). In the n.m.r. spectrum of the anhydro compound, the two singlets at δ 6.12 (H-15) and δ 3.25 (OH at C-14) were absent.

The stereochemistry of the oxygen functions has been established from the n.m.r. spectra of the tetraacetate and of the anhydro-tetraacetate (Table I). The signal of the 7-H, usually found at about δ 4.7 (7,9), appeared at δ 5.12 in the tetraacetate and at δ 4.71 in its anhydro-derivative. This paramagnetic shift of about 0.4 ppm indicates (10) that the 7-H and the 14-OH are in a diaxial 1,3-disposition, and establishes the stereochemistry at the positions 7 (β-H) and 14 (β-OH).

The stereochemistry of the oxygen functions at the positions 1, 2, 11, and 12 has been established in the following way. The doublets at δ 5.24 (J = 8) and at δ 4.77 (J = 2) have been assigned to the 1-H and 12-H, respectively.

TABLE I

Assignments of the NMR Signals of Tetra-O-acetyl- WST-63 and its Anhydro Derivative[a)]

	Tetra-O-acetyl- WST 63	Anhydro derivative
1-H	5.24, d (J = 8)	5.14, d (J = 8)
2-H	ca. 5.40[b)]	ca. 5.36[b)]
3-H	ca. 5.39[b)]	ca. 5.34[b)]
7-H	5.12, t-like	4.71, t-like
11-H	3.85[b)]	3.89, m
11-OH	2.72, d (J = 7)	2.69, d (J = 7.5)
12-H	4.77, d (J = 2)	4.75[b)]
14-OH	3.25, s	---
15-H	6.12, s	---
8-CH_2-O	4.68, d; 3.95, d (J = 8)	4.78, d; 3.70, d (J = 8)
4-CH_3	1.71, s, br	1.69, s, br
10-CH_3	1.46, s	1.46, s
13-CH_3	1.32, s	1.40, s
CH_3COO	2.02; 2.04; 2.07; 2.25	1.98; 2.01; 2.03; 2.23

a) Varian HA-100 in $CDCl_3$, TMS as internal standard, δ-values. Coupling constants (in parentheses) in cps. s = singlet; d = doublet; t = triplet; m = multiplet; br = broad signal.

b) Not clearly resolved signal.

The coupling constant of the hydrogen at C-1 indicates that the hydrogens at C-1 and C-2 must both have an axial or nearly axial disposition and therefore these hydroxyl groups are both equatorial (1β, 2α).

The coupling constant of the hydrogen at C-12 indicates that the 11- and 12-oxygen functions have to be either 11β, 12α or 11α, 12α (11). The pattern of the 11-H signal is best explained if the OH groups are 11β and 12α.

The stereochemistry of the 15-oxygen function has not been established and is assigned to the 15β-position by analogy with other bitter principles of the same family (10).

Acknowledgments: This work was carried out with the support of a research grant AI 7435-01/02 from the U.S. Public Health Service, and a fellowship of the Stiftung für Stipendien auf dem Gebiete der Chemie, Switzerland.

References

1) Contribution No. 2320 from the Department of Chemistry, U.C.L.A.

2) K. Y. Sim, J. J. Sims, and T. A. Geissman, J. Org. Chem., 33, 429 (1968).

3) C.-K. Liang, J. Chinese Chem. Soc., 16,53 (1949); Chem. Abstr. 43, 9377 (1949).

4) Yatanoside, reported (3) m.p. 253-4°, $[\alpha]_D$ + 25.2° (pyridine), purple color with H_2SO_4, was assigned the composition $C_{23}H_{34}O_{10}$ (calc., C, 58.72; H, 7.23; found 58.38; 6.82). For WST-63, calc., C, 58.24; H, 6.84; found, C, 58.12; H, 6.88. Yatanoside acetate, reported m.p. 241-3° $[\alpha]_D$ + 61.7; WST-63 acetate, m.p. 255-256.5°, $[\alpha]_D$ + 42.3. While we are inclined to believe that WST-63 and yatanoside are the same, a direct comparison has not been possible.

5) T. A. Geissman and K. R. Chandorkar, J. Org. Chem., 26, 1217 (1961).

6) J. Polonsky, Z. Basekevitch, A. Gaudemer, and B. C. Das, Experientia, 23, 424 (1967).

7) G. R. Duncan and D. B. Henderson, Experientia, 24, 768 (1968).

8) D.H.R. Barton, S. K. Pradhan, S. Sternhell, and J. F. Templeton, J. Chem. Soc., 1961, 255.

9) J. Polonsky and N. Bouguignon-Zylber, Bull. Soc. chim. France, 1965, 2793.

10) R. C. Sheppard and S. Turner, Chem. Commun., 1968, 77.

11) N. S. Bhacca and D. H. Williams, Application of NMR Spectroscopy in Organic Chemistry, p. 80, Holden-Day, Inc., San Francisco, 1966.

12) G. Kartha and D. J. Haas, J. Am. Chem. Soc., 86, 3630 (1964).

13) Elemental analyses were in agreement with the compositions given.