Tetrahedron Letters No. 8, pp 707 - 710, 1972. Pergamon Press. Printed in Great Britain.

SWAZINE, A NEW ALKALOID FROM SENECIO SWAZIENSIS COMPTON: A CHEMICAL AND X-RAY CRYSTAL STUDY OF A NOVEL SPIRO DILACTONE

By C.G. Gordon-Gray and R.B. Wells

(Department of Chemistry and Chemical Technology, University of Natal,
Pietermaritzburg, South Africa)

and N. Hallak, M.B. Hursthouse, S. Neidle and T.P. Toube

(Department of Chemistry, Queen Mary College, Mile End Road, London, E1 4NS)

(Received in UK 6 January 1972; accepted for publication 19 January 1972)

Extraction[1] of Senecio swaziensis Compton, from Swaziland, yielded two pyrrolizidine alkaloids, retrorsine and a new alkaloid swazine, $C_{18}H_{23}NO_6$, m.p. 165°; $[\alpha]_D^{20}$ - 103.5 (EtOH); λ_{max} (H_2O) 195 nm (ε 11,000).

Hydrolysis of swazine with sulphuric acid (3N) gave the base retronecine (1) and a neutral, mono-unsaturated compound (2), $C_{10}H_{12}O_5$, m.p. 191°; $[\alpha]_D^{20}$ - 116.6° (EtOH); ν_{max} (KBr) 3420 (OH), 1782 and 1771 (C=O), and 1662 (C=C) cm^{-1}; λ_{max} (H_2O) 213 nm (ε 9,700); c.d. $\Delta\varepsilon$ - 8.19 (213 nm). Titration of (2) at room temperature and back titration after refluxing with excess base showed the presence of two lactone rings of different stability; one of these must be α,β-unsaturated (u.v., i.r.). The remaining oxygen in (2) was present as an hydroxyl which was easily acetylated and benzoylated. The n.m.r. spectrum (δ, 100 MHz, $^2H_6$-DMSO) of (2) showed signals for $C\underline{H}_3$-CH (1.17, d, J 7.2 Hz), $C\underline{H}_3$-C (1.37, s), $C\underline{H}$-CH_3 (3.27, q, J 7.2 Hz), $C\underline{H}_2$-O-CO (4.53, ABq), $C\underline{H}_2$=C (5.91, AXq) and O$\underline{H}$ (6.29, s, exchanges with D_2O). In the spectrum of reduced (2) (H_2/Adam's catalyst) the signal for $C\underline{H}$-CH_3 moved to δ 2.4, indicating that this group was adjacent to the carbon-carbon double bond in (2).

Our studies[2] on the mass spectra of the known [e.g. sceleranecic acid (4)[3]] Senecio dilactones showed that (2) was clearly of a novel structure. Dilactones related to (4) lose 44 a.m.u. from the molecular ion in a prominent fragmentation; the mass spectra of (2) and reduced (2) showed no such loss, but their molecular ions lost 88 a.m.u. ($C_3H_4O_3$) instead.

The properties of (2) cannot be explained on the basis of a compound with the carbon skeleton of retronecic acid (5)[4]. However, a compound with the skeleton of (4),but with a double bond at C 1 - C 2 and hydroxyl groups at C 4 and C 7, derived from a C 4 - C 7 epoxide in swazine (6), would have the observed chemical and spectroscopic characteristics. Acid hydrolysis would open the epoxide and the formation of the spiro dilactone (2) would be favoured.

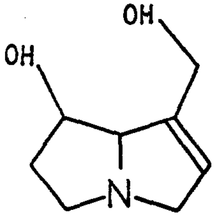
Oxidation of reduced (2) with 1% aqueous potassium permanganate at pH9 yielded a crystalline material m.p. 193° d. and a gummy residue; further oxidation of the latter with hypobromite yielded the expected dimethyl succinic acid (i.r., m.p.). Ozonolysis of (2) yielded formaldehyde and a compound $C_9H_{10}O_6$, m.p. 205°, λ_{max} (H_2O) 243 nm (ε 7.860), a completely enolic β-keto ester. Treatment of (2) with potassium in methanol yielded a crystalline 4-methoxy addition product, m.p. 165°.

Treatment of (2) with *p*-bromobenzoyl chloride in pyridine gave the *p*-bromobenzoate (3). Compound (3) crystallises as colourless needles, in the space group $P2_12_12_1$, with *a*=5.990, *b* = 12.192, and *c* = 22.978 Å, and four molecules in the unit cell. The intensities of 1307 statistically significant reflections were measured on a GE XRD 6 diffractometer, and the structure was solved by the heavy-atom method; the current value of the reliability index is 0.0637. The absolute configuration of the molecule (3*S*, 4*S*, 5*R*) has been determined utilising the anomalous scattering of the bromine atom. The Figure shows a single molecule of (3).

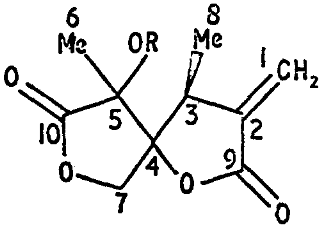
Both lactonic rings are non-planar. The γ-lactone approximates to the customary envelope conformation[5,6] with C 4 displaced from the plane of the other atoms by 0.68 Å. The unsaturated γ-lactone has a half-chair shape, with C 4 and C 3 respectively displaced -0.09 Å and 0.21 Å from the plane through C 2, C 9, and the two oxygen atoms. The conjugated ethylenic and carbonyl double bonds are twisted 8.7° out of plane.

All new compounds gave satisfactory spectra and analyses.

We thank Dr. K. Pachler and Mr. G. Coumbarides for n.m.r. spectra, Dr. S. Eggers and Mr. P. Cook for mass spectra and the South African Council for Scientific and Industrial Research for grants (to C.G.G.-G. and R.B.W.).

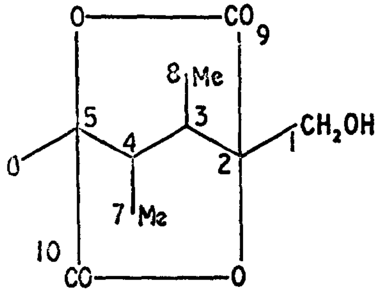


(1)

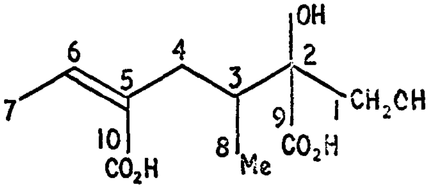


(2) $R=H$

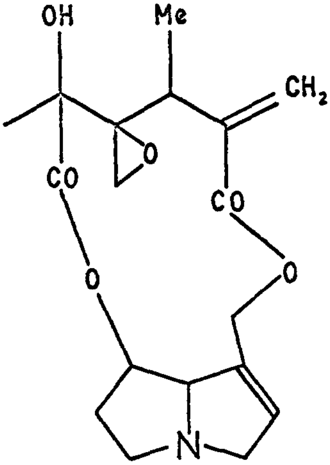
(3) $R=CO-p-C_6H_4Br$



(4)



(5)



(6)

REFERENCES

1 M.J. Koekemoer and F.L. Warren , J. Chem. Soc., 1951, 66

2 To be reported elsewhere.

3 H.L. de Waal, A. Wiechers, and F.L. Warren, J. Chem. Soc., 1963, 953.

4 S.M.H. Christie, M. Kropman, L. Novelli, and F.L. Warren, J. Chem. Soc., 1949, 1703.

5 G.A. Jeffrey and S.H. Kim, Chem. Comm., 1966, 212.

6 T.A. Dullforce, G.A. Sim, and D.N.J. White, J. Chem. Soc. (B), 1971, 1399.

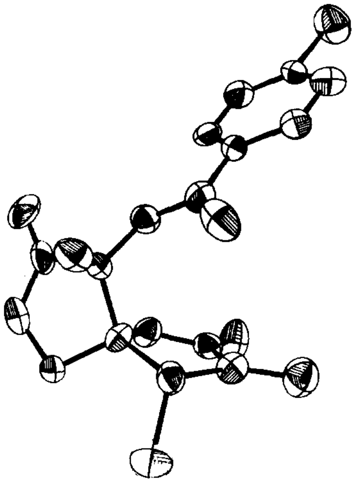


Figure: Thermal Ellipsoid Plot of (3)