Chemical Correlation of Rosein III (11β-Hydroxyrosenonolactone) and Rosenonolactone

By N. KIRIYAMA and Y. YAMAMOTO*

(*Faculty of Pharmaceutical Sciences, Kanazawa University, Takaramachi, Kanazawa-shi, Japan*)

and Y. TSUDA

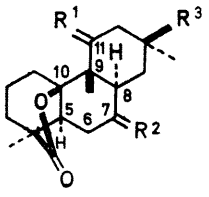
(*Showa College of Pharmaceutical Sciences, Setagaya-ku, Tokyo, Japan*)

Summary The structure and absolute configuration of rosein III (11β-hydroxyrosenonolactone) have been proved by chemically correlating it to rosenonolactone *via* the novel intermediate (**15**); the structure and conformation of isorosein III have also been determined as (**9b**).

THE structure of rosein III was established recently,[1] mainly by an *X*-ray analysis with additional chemical evidence. This prompts us to present independent evidence which leads to the same conclusion by chemically correlating rosein III (**1**) with rosenonolactone (**7**).

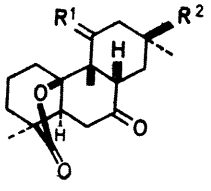
The diketone (**4**), m.p. 214°, prepared by Jones' oxidation of rosein III, formed, by the action of ethanedithiol and BF_3–Et_2O, a dithioacetal (**5**), m.p. 225—226°, which by desulphurization with Raney nickel gave a dihydro-ketone (**6**), m.p. 127—128°, which is different from either dihydrorosenonolactone[2] (**8**) and dihydroisorosenonolactone[3] (**12**). Further thioacetalization of (**6**) was accompanied by opening of the lactone to yield an acid (**13**), m.p. 228°, (methyl ester, m.p. 153°). Desulphurization of (**13**) afforded

an acid, identical with ros-5(10)-en-16-oic acid (**14**)[3] [formerly described as iso(?)rosenoic acid].[4] The identity of the



	R^1	R^2	R^3
(**1**)	α-H, β-OH	O	$CH=CH_2$
(**2**)	α-H, β-OMs	O	$CH=CH_2$
(**3**)	α-H, β-OAc	O	Et
(**4**)	O	O	$CH=CH_2$
(**5**)	O	$-SCH_2CH_2S-$	$CH=CH_2$
(**6**)	O	H_2	Et
(**7**)	H_2	O	$CH=CH_2$
(**8**)	H_2	O	Et

two compounds was confirmed by their i.r. spectra and also those of their methyl esters.

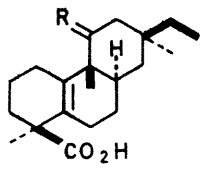


	R^1	R^2
(**9**)	α-H, β-OH	$CH=CH_2$
(**10**)	α-H, β-OAc	$CH=CH_2$
(**11**)	H_2	$CH=CH_2$
(**12**)	H_2	Et

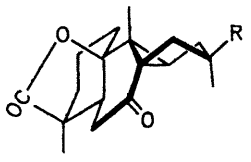
A more elegant correlation was made as follows. Rosein III formed methanesulphonate (**2**), m.p. 145°. On treatment with 0·1% methanolic sodium hydroxide, (**2**) easily lost methanesulphonic acid to give quantitatively, in contrast to $POCl_3$–C_5H_5N dehydration of rosein III,[1] a cyclopropane derivative (**15**), m.p. 175°. Methanesulphonation of isorosein III (**9**),[5] m.p. 166°, gave the same compound directly. The compound (**15**) has no double bond other than the vinyl group which was already present. Other spectroscopic evidence, i.r. (CCl_4), 1687 cm^{-1}; u.v. λ_{max} (EtOH) *ca.* 210 nm, log ε 3·60, indicates that the cyclopropyl group is conjugated to the ketonic function. The strong negative Cotton effect ($a = -62$) of this compound showed that the cyclopropyl group has the stereochemistry[6] illustrated. Hydrogenation of (**15**) gave a dihydro-derivative (**16**), m.p. 148—150°. Further hydrogenation under forcing conditions, (60°, 12 h with a large excess of palladium–charcoal), opened the cyclopropane ring to give a 1 : 1 mixture of dihydrorosenonolactone (**8**),[2] m.p. 188°, and dihydroisorosenonolactone (**12**),[2] m.p. 142°. The identities of these compounds were confirmed by direct comparison with the authentic samples.

The hydroxy-group in rosein III is equatorial since the geminal proton to the hydroxy-group appeared as a quartet (J 10 and 8 Hz) at δ 4·13 p.p.m. Dihydrorosein III acetate (**3**) showed a much clearer pattern, δ 5·16 p.p.m. q, J 12 and 6 Hz).

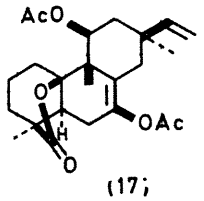
The hydroxy-group in isorosein III (**9**) is also equatorial, δ 4·15 p.p.m. q, J 16 and 6 Hz. Acetylation of this gave a mixture of a normal acetate (**10**), m.p. 144°, δ 5·53 p.p.m. (>C*H*–OAc, J 10 and 6 Hz), and an enol-acetate (**17**), m.p. 154—155°, (no vinyl H except $-CH=CH_2$ in the n.m.r. spectrum).



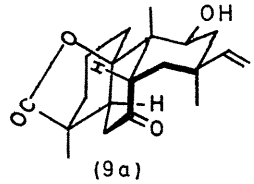
(**13**) R = $-SCH_2CH_2S-$
(**14**) R = H_2



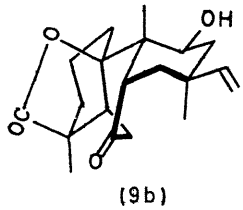
(**15**) R = $CH=CH_2$
(**16**) R = Et



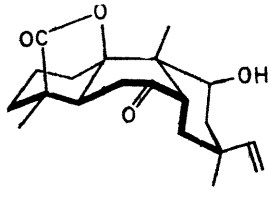
(**17**)



(**9a**)



(**9b**)



(**9c**)

Isorosein III and isorosenonolactone differ in their stability. The equilibration of rosein III and isorosein III by 0·1% MeOH–NaOH, where the γ-lactone remained unaffected, favoured the formation of rosein III showing that the iso-compound is less stable, while rosenono- and isorosenono-lactone appeared to have approximately equal stability.[3] On the contrary, both rosein III and rosenonolactone were irreversibly converted into iso-series by the strong alkaline conditions in which the γ-lactone is opened.[3–5] The destabilization of isorosein III is probably due to the non-bonded interaction between the 1α-H and the 11β-OH, which would cause some conformational changes in ring B compared to isorosenonolactone for which the chair form (**9a**; H instead of OH) has been suggested[3–7] In fact, the o.r.d. curve of isorosein III ($a = +73$) was profoundly different from that of isorosenonolactone ($a = -29$),[7] whilst the similar curves of rosein III and rosenonolactone imply the same conformation of the two original compounds. Therefore the (half) boat conformation (**9b**), which should give a strong positive Cotton effect in the octant projection, is suggested for isorosein III, giving some relief of the interaction between 1α-H and 11β-OH. The increased interaction between 6α-H and

13-MeO will be compensated by decrease of the interaction between the 7-oxo-group and 13-Me The alternative conformation (**9c**)† is unlikely, since the hydroxy-group was shown to be equatorial (see above)

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† Stabilization due to OH to π (of the vinyl group) bonding in conformation (**9c**) was suggested by a referee, but we have found that acetylisorosein III had the same positive o r d ($a = +65$) where OH to π bonding is absent

[1] R Guttormson, P Main, A J Allison, and K H Overton, *Chem Comm*, 1970, 719.
[2] A Robertson, W R Smithies, and E Tittensor, *J Chem Soc*, 1949, 879
[3] G A Ellestad, B Green, A Harris, W B Whalley, and H Smith, *J Chem Soc*, 1965, 7246
[4] A Harris, A Robertson, and W B Whalley, *J Chem Soc*, 1958, 1799
[5] G G Freeman, R I Morrison, and S E Michael, *Biochem J*, 1949, **45**, 191
[6] T Norin, *Acta Chem Scand*, 1963, **17**, 738
[7] C G Grazia, W Klyne, P M Scopes, D R Sparrow, and W B Whalley, *J Chem Soc* (*C*), 1966, 896.