Constitutions of Rubrenolide and Rubrynolide: an Alkene–Alkyne Pair from *Nectandra rubra*

By N. C. Franca and O. R. Gottlieb

(*Laboratório de Produtos Naturais da Fundação de Amparo à Pesquisa do Estado de São Paulo, Universidade de São Paulo, Brasil*)

and D. T. Coxon and W. D. Ollis*

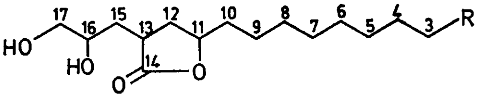
(*Department of Chemistry, The University, Sheffield* S3 7HF)

Summary Constitutions are proposed for rubrenolide (Ia) and rubrynolide (Ib), two structurally novel natural products isolated from *Nectandra rubra* (Lauraceae).

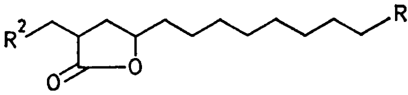
The trunk wood of the Amazonian tree, *Nectandra rubra* (Mez) C. K. Allen[1] of the Lauraceae family has yielded rubrenolide and rubrynolide which represent a novel natural product type.

Rubrenolide (Ia), $C_{17}H_{30}O_4$, m.p. 100°, $[\alpha]_D + 21°$, ν_{CO} 1745 cm^{-1}, was identified as a terminal alkene which, on the basis of i.r. and n.m.r. evidence, is associated with a $-CH_2-CH{=}CH_2$ group. Rubrynolide (Ib), $C_{17}H_{28}O_4$, m.p. 88°, $[\alpha]_D + 21°$, ν_{CO} 1745 cm^{-1}, was similarly shown to be the corresponding terminal alkyne containing a $-CH_2-C{\equiv}CH$ group. On catalytic hydrogenation rubrenolide and rubrynolide each gave dihydrorubrenolide (Ic), $C_{17}H_{32}O_4$, m.p. 106—107°, $[\alpha]_D + 22°$. The two hydroxy-groups present in rubrenolide were shown, using trichloroacetyl isocyanate,[2] to be primary and secondary, and their vicinal relationship was established by periodate cleavage of dihydrorubrenolide which gave formaldehyde and an aldehyde, $C_{16}H_{28}O_3$, m.p. 50—53° (ν_{CO} 1760 and 1720 cm^{-1}). Intramolecular hydrogen bonding made a direct deduction of the lactone ring size in rubrenolide uncertain (ν_{CO} 1745 cm^{-1}), but the acetonide, $C_{20}H_{36}O_4$, m.p. 47—48°, prepared from dihydrorubrenolide, acetone, and anhydrous copper sulphate was clearly a γ-lactone (ν_{CO} 1770 cm^{-1}). The C_{17}-skeleton of rubrenolide was determined by transforming dihydrorubrenolide to 4-methylhexadecane (III) by the sequence: (i) reduction ($LiAlH_4$), (ii) formation of a tetramesylate, and (iii) hydrogenolysis ($LiAlH_4$). Vigorous oxidation of rubrenolide with chromium trioxide in boiling acetic acid gave sebacic acid, $HO_2C[CH_2]_8CO_2H$. Thus, two possible constitutions (IIa) or (IIb) could be considered for rubrenolide, and a decision between these was possible on the following evidence. Mild oxidation of rubrenolide (CrO_3–HOAc; room temp.) yielded a vinylic ($\nu_{C=C}$ 1645, 990, and 910 cm^{-1}) lactonic acid (ν_{CO} 1760 and 1700 cm^{-1}), $C_{16}H_{26}O_4$, m.p. 95—98° (IIc), whose n.m.r. spectrum showed an ABX system (H_A τ 7·05, H_B τ 7·49, H_X m, τ *ca.* 7·0; J_{AB} 17·5, J_{AX} 3·5, and J_{BX} 8·5 Hz) which had to be associated with the oxidatively generated carboxy-group ($HO_2C-CH_AH_B-CH_X<$). A corresponding ABX system was also identifiable in the n.m.r. spectrum of the lactonic acid methyl ester (IId).

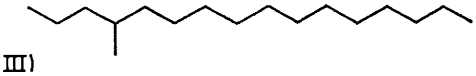
These results established the constitutions of rubrenolide (Ia) and rubrynolide (Ib) and these proposals were fully confirmed by examination of the high resolution mass spectra and n.m.r. spectra of the two compounds and their derivatives. The assignment (Table) of seven 1H multiplets observed in the 220 MHz n.m.r. spectrum (CD_3OD-D_2O) of dihydrorubrenolide (Ic) was made possible by spin-decoupling experiments.



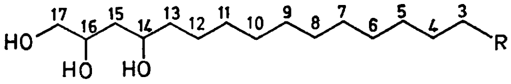
(Ia) Rubrenolide R = $CH_2{=}CH$
(Ib) Rubrynolide R = $CH{\equiv}C$
(Ic) Dihydrorubrenolide R = CH_3-CH_2



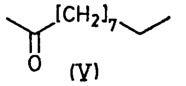
(IIa) $R^1 = CH_2{=}CH$; $R^2 = HO{\cdot}CH_2{\cdot}CH(OH)$
(IIb) $R^1 = HO{\cdot}CH_2{\cdot}CH(OH)$; $R^2 = CH_2{=}CH$
(IIc) $R^1 = CH_2{=}CH$; $R^2 = CO_2H$
(IId) $R^1 = CH_2{=}CH$; $R^2 = CO_2Me$



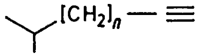
(III)



(IVa) Avocadene R = $CH_2{=}CH$
(IVb) Avocadyne R = $HC{\equiv}C$



(V)



(VI) $n = 7$
(VII) $n = 9$, probable structure

N.m.r. spectrum (220 MHz) *of dihydrorubrenolide* (Ic)

τ	Multiplicity	Assignment
8·02	Octet, J 14·5, 10, 5 Hz	H_A at C-15[a]
7·45	Octet, J 12·5, 8·5, 5·5 Hz	H_A at C-12[a,b]
7·06	Complex	H at C-13
6·51	Double d, J 11, 6·5 Hz	H_B at C-17
6·38	Double d, J 11, 3·5 Hz	H_A at C-17
6·28	Complex	H at C-16
5·54	Complex	H at C-11

[a] H_B at C-15 and H_B at C-12 are obscured by the $[CH_2]_8$ signals which extend down to τ 8·2. [b] Double irradiation at τ 5·54 produced only one clearly observable change in the spectrum: the signal at τ 7·45 changed to a double d (J 12·5, 8·5 Hz).

The branched chained C_{17}-compounds, rubrenolide (Ia) and rubrynolide (Ib) from *Nectandra rubra* (Lauraceae) show an interesting biogenetic relation to the family of structurally related linear C_{17}-compounds [*e.g.* (IVa) and (IVb)] recently isolated from the seed of the avocado pear, *Persea americana* (Lauraceae).[3,4] A proposed phytochemical relation[4,5] between these two classes of C_{17}-compounds isolated from Lauraceae may be extended to include some C_{11}- and C_{13}-compounds, (V)—(VII) from *Litsea odifera*.[6] The natural products (Ia), (IIa), (IVa), (IVb and related compounds[4]), (V), (VI), and (VII) may all be derived as biosynthetic variants upon the acetate–malonate route to saturated fatty acids;[7] the biogenetic correlation between the natural product types (I) and (IV) is indicated by numbers.

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