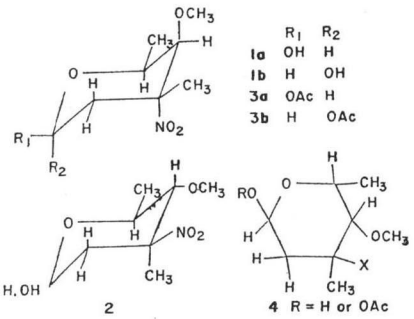
THE CHEMISTRY OF RUBRADIRIN. II RUBRANITROSE

Sir:

Rubradirin[1~4] contains a $C_8H_{15}NO_5$* moiety not found in rubradirin B[5]. We here report that acid hydrolysis of rubradirin afforded this fragment which was found to be a nitrosugar we have named L-rubranitrose. L-Rubranitrose is shown to have structure **1a**. It is stereoisomeric with evernitrose, **2**[6,7], found in the unrelated antibiotics, everninomicins B and C.

Anomeric **1a, b** was separated from the second component of the hydrolytic mixture, acidic rubradirin aglycone, by distribution of the former into the chloroform layer of a 2-phase system which also contained a 5% Na_2CO_3 solution. The two anomers were distinguished by C-1 proton signals at δ 4.75 and δ 5.28. After chromatography, the latter was crystallized, mp



* The analytical values are consistent with these molecular formulas.

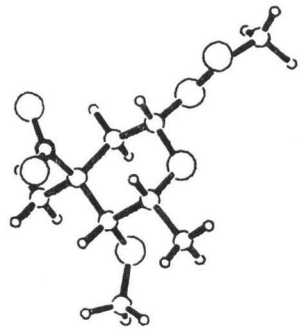
150~153°, $[\alpha]_D$ +127° → +86° (*c* 1, ethanol). Acetylation of the mixture in acetic anhydride and pyridine afforded anomeric 1-acetyl rubranitrose, from which we were able to crystallize the opposite anomer, **3a**, mp 74~76°, $[\alpha]_D$ +36° (*c* 0.4, ethanol). The ^1H NMR signal of its C-1 proton showed that this was the anomeric configuration in the rubradirin glycoside (see Table 1). A further analysis of the proton spectra of **1** and **3** accounted for all of the carbons and hydrogens in three segments, O–CHCH$_2$–C(=O)–, O–CHCH$_3$CHOCH$_3$C–, and CCH$_3$X. The combination of these fragments into a pyranose, **4** accounted for all atoms save a nitrogen and 2 oxygens, suggesting that "X" was a nitro group. An infrared band at 1550 cm^{-1} and evolution of NO_2 upon heating supported this assumption.

The differences in the proton NMR spectra of **3a** and **3b** seemed to favor the indicated relative stereochemistry if we arbitrarily specified a 1-C conformation of the pyranose. The axial C-1 proton in **3a** is seen in its 9.8-Hz coupling with H_{ax} on C-2. Long range coupling of H_{eq} (C-2) with H(C-4) is satisfied by the coplanar system H_{eq}(C-2)(C-3)(C-4)H_{eq}-4 which exists in this configuration. In **3b** an axial acetyl function would receive maximum shielding if the nitro group at C-3 were also axial, accounting for the significant upfield shift of its three protons relative to those in **3a**. This diaxial interaction appears to affect other ring substituents as well,

Table 1. ^1H-NMR spectra of rubranitrose compounds shift in ppm, number of protons, appearance, coupling in Hz.

C No.	No. Protons	Compound **1b**	Compound **3a**	Compound **3b**
1	1	5.28, DD, J_{2ax} 2.5, J_{2eq} 3.5	5.73, DD, J_{2ax} 9.8, J_{2eq} 3.5	6.1, DD, J_{2ax} *ca* 3.5, J_{2eq} *ca* 2
1a	3		2.09, S	1.94, S
2 ax	1	2.05, DD, J_{2eq} 14.5, J_1 2.5	1.97, DD, J_{2eq} 14.5, J_1 9.8	2.14, DD, J_{2eq} 14.5, J_1 *ca* 3.5
2 eq	1	2.67, DD J_{2ax} 14.5, J_1 3.5	2.52, DDD, J_{2ax} 14.5, J_1 2.4, J_4 1.5	2.73, DD, J_{2ax} 14.5, J_1 *ca* 2, J_4 ?
3a	3	1.67, S	1.69, S	1.64, S
4	1	3.71, BrS, J_5<1	3.63, M	3.74, Br S, J_5<1
4a	3	3.62, S	3.65, S	3.60, S
5	1	4.40, Br Q, $J_6$6.5, J_4<1	3.63, M	4.24, Br Q, $J_6$6.5, J_4<1
6	3	1.33, D, $J_5$6.5	1.33, D, $J_5$6.5	1.33, D, $J_5$6.5

Fig. 1. Computer drawing of **3a**.



especially the proton at C-5. This group would most likely be equatorial.

These speculations were confirmed by a crystallographic study of **3a**, which produced the structure shown in Fig. 1.

The crystals are monoclinic, space group P_{2_1}, with unit-cell parameters: $a=8.528$ (0.001)Å, $b=13.133$ (0.001)Å, $c=11.741$ (0.001)Å, $\beta=112.38$ (0.01)°. Intensity data on the 2286 reflections with $2\theta \leq 138°$ were collected at low temperature (−155°C) using a Syntex $P\bar{1}$ diffractometer controlled by an IBM 1800 computer using graphite monochromatized CuKα radiation ($\lambda=1.5418$Å). The structure was solved by direct methods using DIREC II and was refined by crystallographic least squares.

The final agreement index R,

$$\left(R=\sum\left||F_o|-|F_c|\right|\Big/\sum|F_o|\right), \text{ was } 0.033.$$

The standard deviation of fit

$$\left[\text{for G.O.F.}=\left(\frac{\sum w(|F_o|^2-|F_c|^2)^2}{m-s}\right)^{1/2}\right]$$

was 4.5. All calculations were carried out on an IBM 370 computer using the CRYM crystallographic system of crystallographic programs developed by D. J. DUCHAMP of these laboratories.

The absolute configuration was established by a comparison of the circular dichroism of **3a** with that of evernitrose, **2**.[7] The compounds showed oppositely signed COTTON curves in the vicinity of the 280 nm nitro group[8] electronic transition. The molar ellipticity in methanol at 285 nm was +2500 for **3a** and −1200 for **2**. If it is assumed that the sign of the CD near 280 nm is determined mostly by the absolute configuration at C-3, then **3a** and **2** have opposite absolute configurations at C-3, R for **3a** and S for **2**. Thus, **3a** has the absolute configuration as shown and belongs to the L-series as does evernitrose.

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