Solution Structure and Assignments of the ^{1}H and ^{13}C NMR Spectra of Erythromycin C in Organic and Aqueous Solution

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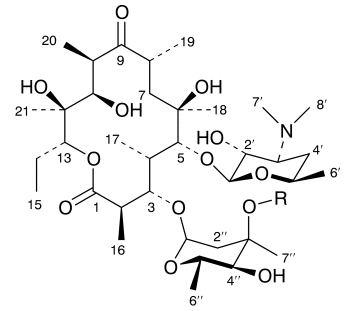
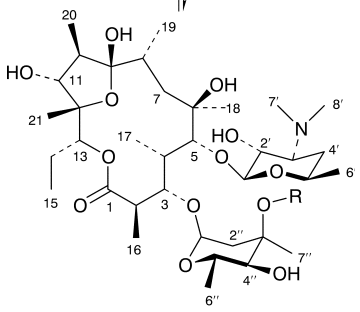
Erythromycin C (**1**) has been shown to exist as a 4:5 equilibrium mixture of the 9-ketone and 12,9-hemiacetal ring-chain tautomers in aqueous solution at ambient temperature.

Erythromycin C (**1**) is a biosynthetic precursor of the important macrolide antibiotic erythromycin A (**2**). Like erythromycin A, erythromycin C is active against a broad range of Gram positive bacteria. Both antibiotics exert their antibacterial action by binding to the 50 S ribosomal subunit, thereby inhibiting bacterial protein synthesis.



1a R = H
2a R = CH_3



1b R = H
2b R = CH_3

It has been shown previously that in aqueous solution at ambient temperature, apparent pH 7.4, erythromycin A exists as a 5:2 mixture of the 9-ketone (**2a**) and the 12,9-hemiacetal (**2b**).[4] We have now fully assigned the ^{1}H and ^{13}C NMR spectra of erythromycin C in buffered D_2O and $[^{2}H_4]$methanol and shown that, for erythromycin C, the hemiacetal is relatively abundant. The ratio of ketone: hemiacetal in aqueous buffer is 4:5 at room temperature, rising to 2:1 at 60 °C. In $[^{2}H_4]$methanol at room temperature the ratio is 7:4 in favour of the ketone.

Cyclised derivatives of the macrolide antibiotics appear not to have antibacterial activity.[9–11] The presence of a relatively large proportion of hemiacetal may in part explain the low antibacterial activity of erythromycin C relative to erythromycins A and B.

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Techniques used: ^{1}H and ^{13}C NMR

References: 13

Fig. 1: HMBC spectrum of erythromycin C in $[^{2}H_4]$methanol solution

Table 1: Assignments if the ^{1}H and ^{13}C NMR spectra of erythromycin C in $[^{2}H_4]$methanol

Table 2: Assignments if the ^{1}H and ^{13}C NMR spectra of erythromycin C in buffered D_2O

Table 3: Key chemical shift changes in erythromycins A and C in aqueous solution

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