Communication to the editor

THE BIOSYNTHESIS OF PICROMYCIN USING ^{13}C ENRICHED PRECURSORS

Sir:

Using ^{13}C enriched precursors it has been elucidated recently[1] that the aglycone of the leucomycins was derived from five acetates, one propionate, one butyrate and an unknown C_2-unit corresponding to carbons-3 and -4. In the case of magnamycin which is C-9 oxidation product of leucomycin, previous studies using ^{14}C labeled precursors[2] suggested an acetate origin for carbons-3 and -4. Another biosynthetic investigation on the 16-membered macrolide antibiotic tylosin[3] afforded evidence that carbons-3, -4 and -18 of this compound were originating from a propionate unit. Taking an interest in whether the aglycone of a 14-membered macrolide has such biogenetically unknown carbons, an investigation with picromycin as an example was undertaken. In the biosynthesis of erythromycin, it has been well established that 27 carbons of its aglycone are derived from seven propionates.[4]

Although propionate and acetate have been estimated in many articles to be precursors for aglycone of picromycin,[4~6] there is not enough evidence to support this speculation. In this paper we report the incorporation pattern of [1-^{13}C]-acetate and [1-^{13}C] propionate into picromycin.

Streptomyces flavochromogenes, a picromycin-producing strain, was inoculated into a seed medium containing 2% glucose, 0.5% meat extract, 0.5% peptone, 0.1% yeast extract, 0.5% NaCl and 0.3% $CaCO_3$ and cultivated on a reciprocal shaking machine at 27°C. A 48-hour culture was transferred into a picromycin-producing medium containing 1% starch, 1% yeast extract, 1% casamino acids and 0.5% $CaCO_3$, and it was fermented at 27°C. After 8 hours, each of ^{13}C-labeled precursors was added and the fermentation was continued for an additional 26~30 hours. The culture filtrates (500 ml) were then extracted with chloroform at pH 8.0 and the extracts were concentrated to dryness. The crude materials containing picromycin were chromatographed over silica gel thin-layer

Fig. 1. ^{13}C-NMR spectra of picromycin

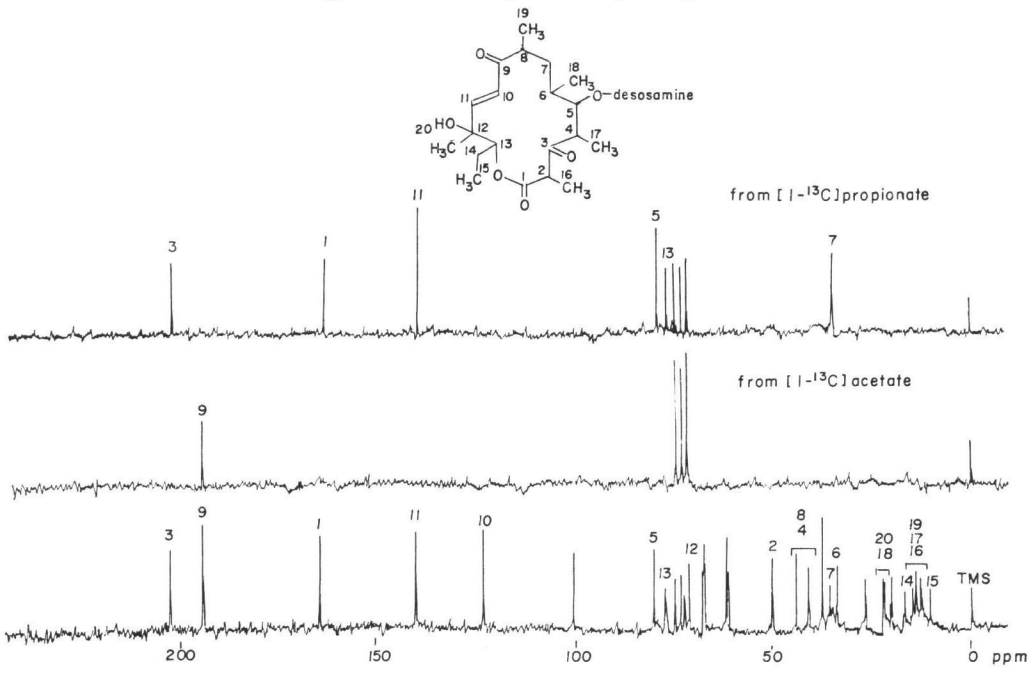
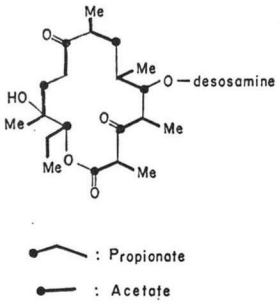


plate using chloroform - methanol (5:1) as a developer to isolate pure picromycin (200 mg). The ^{13}C-NMR spectra in $CDCl_3$ at 22.63 MHz of the labeled and cold picromycins are illustrated in Fig. 1. The assignments of the signals in the ^{13}C-NMR spectra result from our previous report.[7]

When [1-^{13}C] propionate was added, as expected, carbons-1, 3, 5, 7, 11 and 13 were enriched. On the other hand, after the addition of [1-^{13}C] acetate, only carbon-9 was enriched. From these results, the incorporation pattern of these building units into the aglycone of picromycin was confirmed as shown in Fig. 2.

Fig. 2. Biosynthesis of picromycin
Closed circle indicates the position of carboxyl carbon enriched by ^{13}C.



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