Tetrahedron Letters No. 15, pp 1367 - 1368, 1974. Pergamon Press. Printed in Great Britain.

# CARBON-13 NMR SPECTRUM OF RIFAMYCIN S: A RE-EXAMINATION OF THE ASSIGNMENTS WITH SPECIAL REFERENCE TO THEIR BIOGENETIC IMPLICATION.

E. Martinelli, R.J. White and G.G. Gallo
Laboratori Ricerche Lepetit S.p.A., 20158 Milano, Italy

P.J. Beynon
Jeol Ltd., London N.W. 9, England

(Received in UK 12 February 1974; accepted for publication 4 March 1974)

In a previous paper we reported the $^{13}C$ NMR spectrum of rifamycin S and the attribution of the majority of the 37 carbon atoms present[1]. This work was the starting point for a study of the biosynthesis of rifamycin S using $^{13}C$ enriched precursors[2]. Assignments within three groups of carbon atoms were only tentative as the necessary $^{1}H$ selective decoupling experiments were only performed in the case of C-17 and C-19 which had a decisive biogenetic implication. Fortunately, carbons of the same group have the same metabolic origin and these uncertainties did not affect the biosynthetic argument. Therefore, a checking of our tentative assignments by exhaustive $^{1}H$ selective decoupling was postponed. Meanwhile, a paper by Fuhrer[3] has appeared also reporting the $^{13}C$ NMR spectrum of rifamycin S and utilizing this latter approach extensively. The two published sets of assignments[1,3] do not agree on certain points. In particular, two of these attributions, namely C-6 and C-8, are of crucial biogenetic importance. The purpose of this letter is a critical evaluation of the discrepancies.

In Fig. 1 the structure and the FT proton-decoupled $^{13}C$ spectrum of rifamycin S in $CDCl_3$ is reported, together with our revised assignments based on $^{1}H$ selective decoupling. By comparing them with those previously reported by us[1] and by Fuhrer[3] it can be observed that: 1) our present assignments of the proton bearing carbons agree perfectly with those given by Fuhrer and consequently some of our previous ones must be changed; 2) with the exception of C-6 and C-8, we also agree with the assignments of the quaternary carbons reported by this author and consequently our previous attributions for C-2, C-9 and C-10 must be changed.

The choice between C-6 and C-8 has been investigated by performing $^{1}H$ selective decoupling on 25-desacetyl rifamycin S, where overlapping due to the signal of C-35 is absent. This experiment clearly shows that irradiation at the $^{1}H$ NMR frequency of the OH on C-8 at 12,50 ppm[4] results in a definite enhancement of the

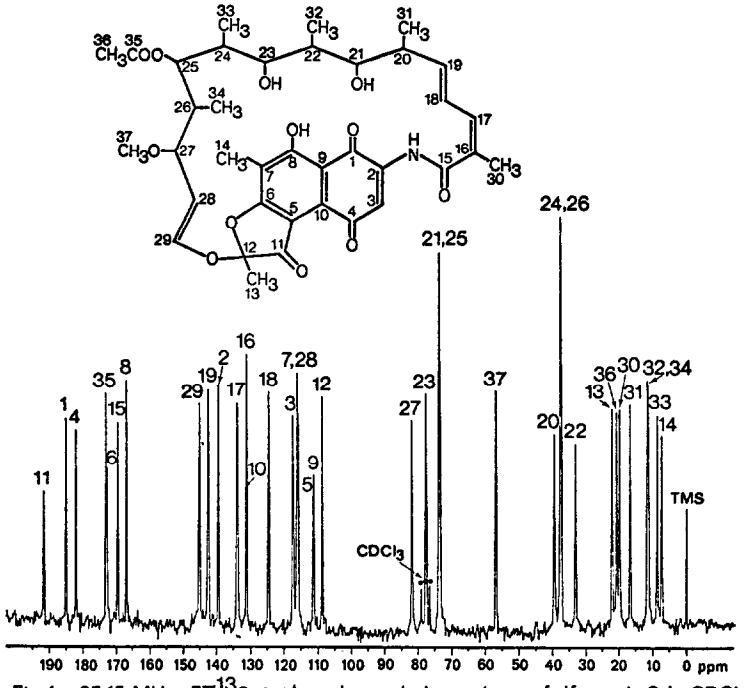


Fig.1 25.15 MHz - FT $^{13}C$ proton-decoupled spectrum of rifamycin S in $CDCl_3$

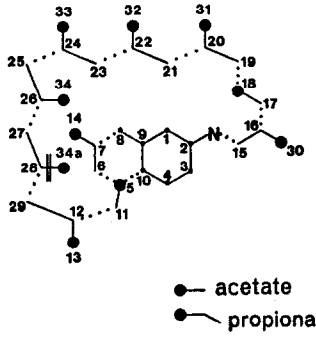


Fig. 2 - Alignment of acetate and propionate units in rifamycin carbon skeleton. Carbon 34a is lost during biosynthesis[2].

$^{13}C$ signal at 166.8 ppm only, indicating the removal of the $^{2}J$ C-O-H coupling and thus confirming our previous assignments. The importance of a correct assignment for C-6 and C-8 is evident from the biogenetic scheme presented in fig. 2[2]. The assignment reported by Fuhrer would no longer permit the construction of the rifamycin carbon skeleton from a continuous condensation of eight propionate and two acetate units in a single polyketide chain initiated by a seven carbon amino moiety.

## REFERENCES

(1) E. Martinelli, R.J. White, G.G. Gallo and P.J. Beynon, Tetrahedron, 29, 3441 (1973).
(2) R.J. White, E. Martinelli, G.G. Gallo, G. Lancini and P.J. Beynon, Nature Lond., 243, 273 (1973).
(3) H. Fuhrer, Helv. Chim. Acta, 56, 2377 (1973).
(4) W. Oppoltzer and V. Prelog, Helv. Chim. Acta, 56, 2287 (1973).