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STUDIES ON JULIMYCINS—VII

THE STRUCTURES OF JULICHROMES $Q_{1\cdot 6}$, $Q_{6\cdot 6}$ AND $Q_{5\cdot 6}$

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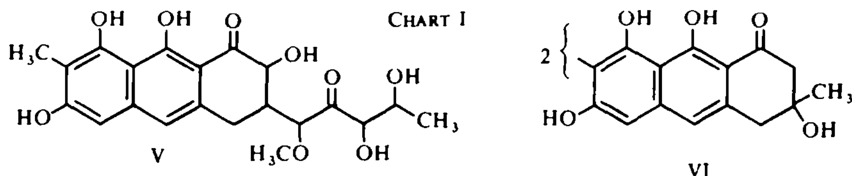
Abstract—The structures of three julichromes which have a new Q_6 unit have been elucidated. Since the Q_6 unit, a derivative of 8,9-dihydroxy-1-oxo-1,2,3,4-tetrahydroanthracene, is closely related to the Q_1 unit, julichromes $Q_{1\cdot 6}$ and $Q_{6\cdot 6}$ are of interest in connection with the biogenesis of julimycin B-II.

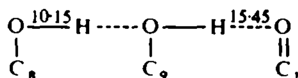
THE isolation[1] of about twenty new pigments from the coloured metabolites (julimycin B-complex) of *Streptomyces shiodaensis* and the structures[2-4] of eleven of the compounds have been reported. This paper is concerned with the structures of julichromes $Q_{1\cdot 6}$, $Q_{6\cdot 6}$ and $Q_{5\cdot 6}$.

Julichrome $Q_{1\cdot 6}$ (I) has a molecular formula, $C_{38}H_{36}O_{13}$, and the presence of the known Q_1 unit (cf. Chart 1) in the molecule is clear from the assignment of its NMR spectrum* (*cf* Fig 1). Since all the compounds which are composed of a Q_1 unit and



one of the known units ($Q_1 \sim Q_5$) have been established, I must include a new unit in its molecule. In accordance with this presumption, the NMR signals attributable to the unknown part are not identical with those of the known units.

The new Q_6 unit, however, should have a ring system similar to those of the known units on account of its formula, $C_{19}H_{19}O_6$, and its NMR pattern. The substituents on the hydroaromatic ring (ring A) of the Q_6 unit should be identical with those of the Q_1 unit because of the similar pattern of the signals, also the conformations may be the same. The AB-type quartet centered at 7·50 ppm (J = 8·0 c/s) suggests the presence of two *ortho* protons on the aromatic ring (ring C) as in other known units. Different from the other units the B-ring of the Q_6 unit must be aromatic, because the spectrum reveals the additional one aromatic proton signal at 7·15 ppm (singlet) and two phenolic OH proton signals at 15·45 and 10·15 ppm. Since the two phenolic OH proton signals show a significant downfield shift due to chelation, the location of the phenolic OH groups at C_8 and C_9 is required. The chelation feature, is in good



* NMR spectra were taken with a Varian A-60 spectrometer. Chemical shifts are expressed in δ(ppm) downfield from TMS used as internal reference.

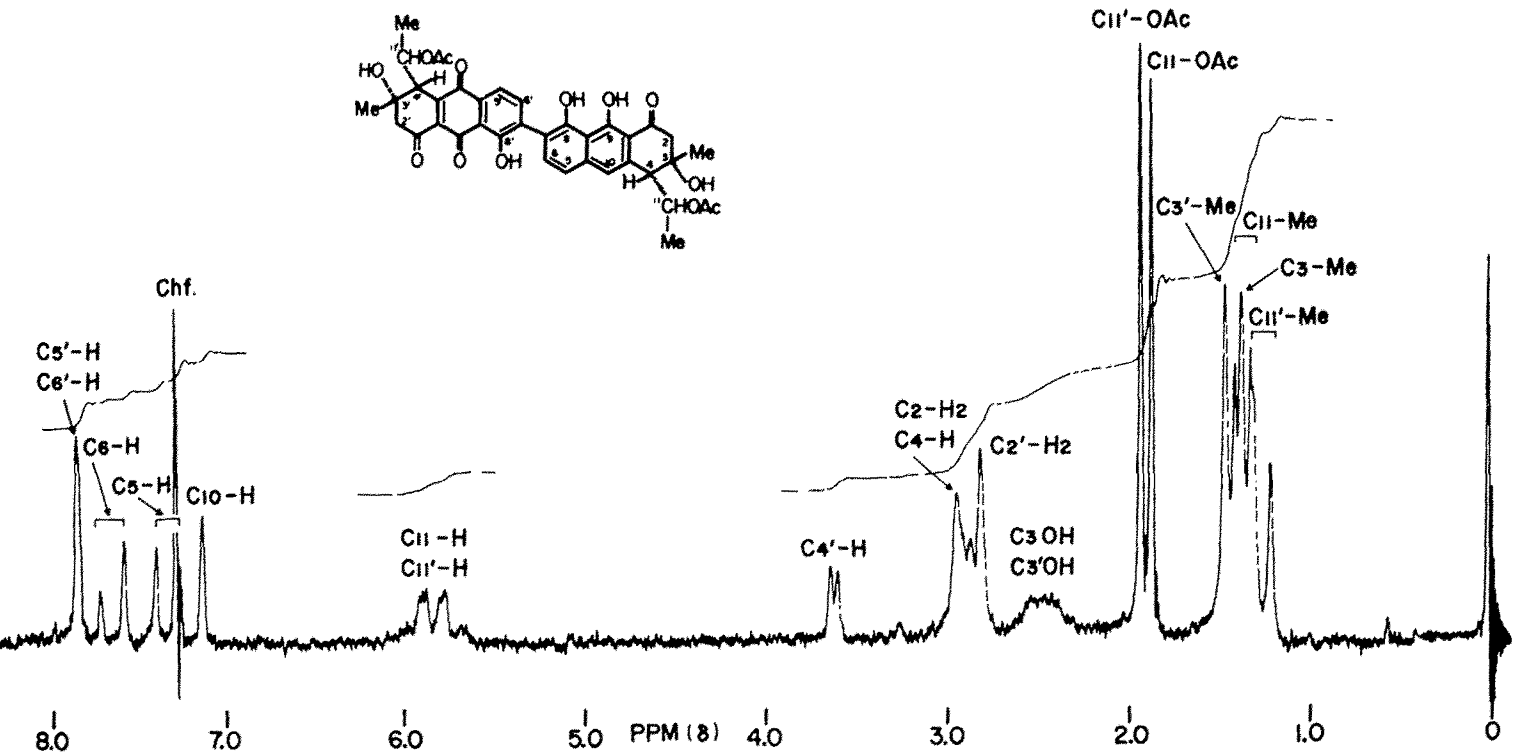


FIG 1. NMR spectrum of I

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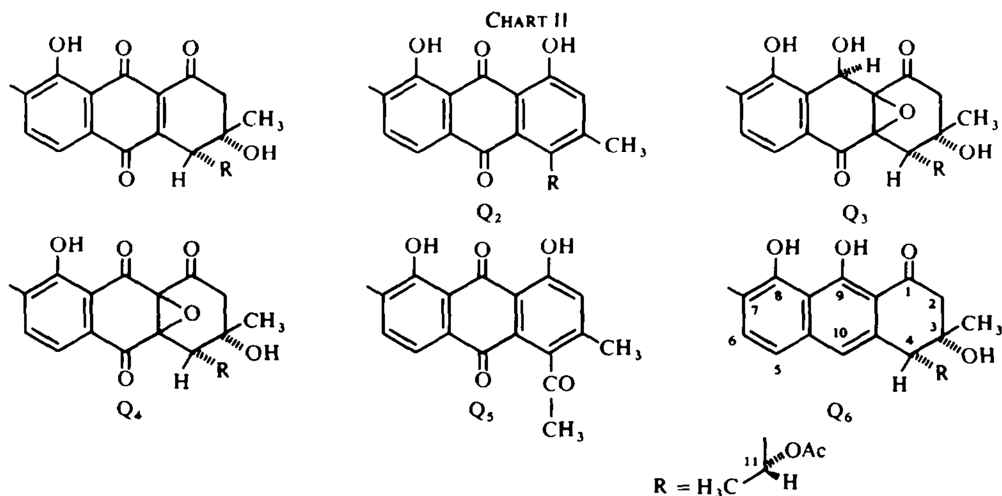
In this structure, the upfield shift of C_5—H, C_6—H and C_4—H signals and the downfield shift of C_{11}—CH_3 signal, compared with those of the Q_1 unit, are reasonably explained by the absence of the CO function at C_{10}.

In order to confirm the structure by the chemical correlation with julimycin B-II (Q_1—Q_1), I was oxidized with Fremy's salt and with chromic acid. Both reactions gave the same result, and the formation of julimycin B-II was ascertained by continuous development TLC on acidic silica gel and by ordinary TLC on silica gel G using julimycin B-II as reference, but the yields were too poor for further identification. The absolute configuration, therefore, could not be ascertained, though it may be the same as those of other units from the biogenetic point of view.

The main product of the oxidation of I was easily established as II (*cf* Chart 2), oxidized at the C ring to the quinone system, by the assignment of its NMR spectrum (*cf* Fig 2).

CHART II



Acetylation of I with acetic anhydride-pyridine gave 8,8'-O-diacetate. However, the oxidation of the acetate to 8,8'-O-diacetyl julimycin B-II was unsuccessful, because on treating with above oxidants the starting material was completely recovered. The inertness of the C_9—OH group may be attributed to its being strongly masked by the neighbouring two O-functions.

Julichrome $Q_{6\cdot6}$ (III) is a pigment which is negative to the colour reaction with magnesium acetate. Therefore, III probably has no peri-hydroxy quinonoid chromophore. Moreover, its behaviour on TLC, III $\geqq$ I (Q_1—Q_6) $\geqq$ julimycin B-II (Q_1—Q_1) (on acidic silica gel) and III $\ll$ I $\ll$ julimycin B-II (on silica gel G), suggests that III consists of two Q_6 units.

As expected, the elementary analysis gave the molecular formula, $C_{38}H_{38}O_{12}$, and its NMR showed only the signals attributable to the Q_6 unit giving III the structure, Q_6—Q_6.

Julichrome $Q_{5\cdot6}$ (IV) is a component occuring naturally to only a slight extent.

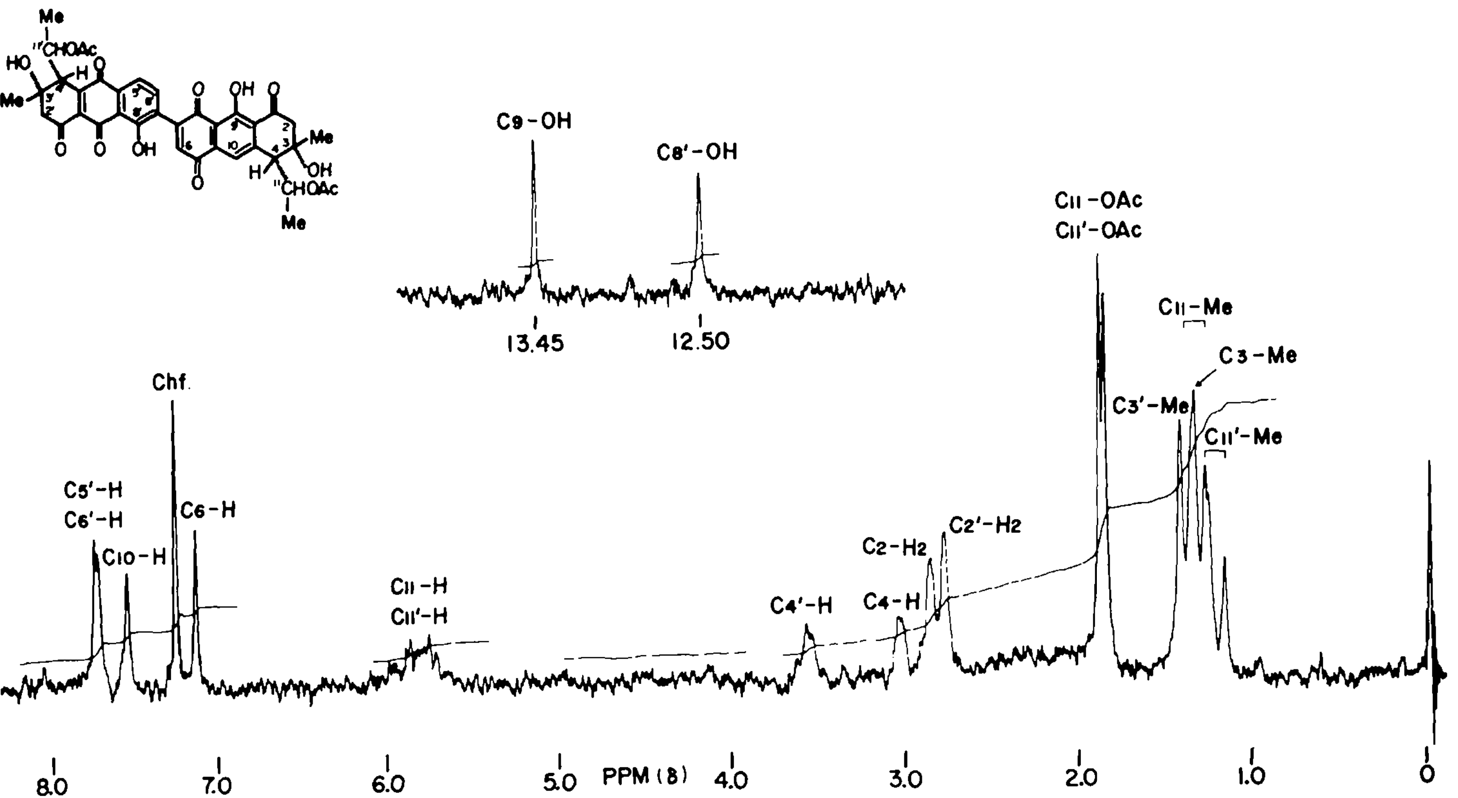


FIG 2. NMR spectrum of II

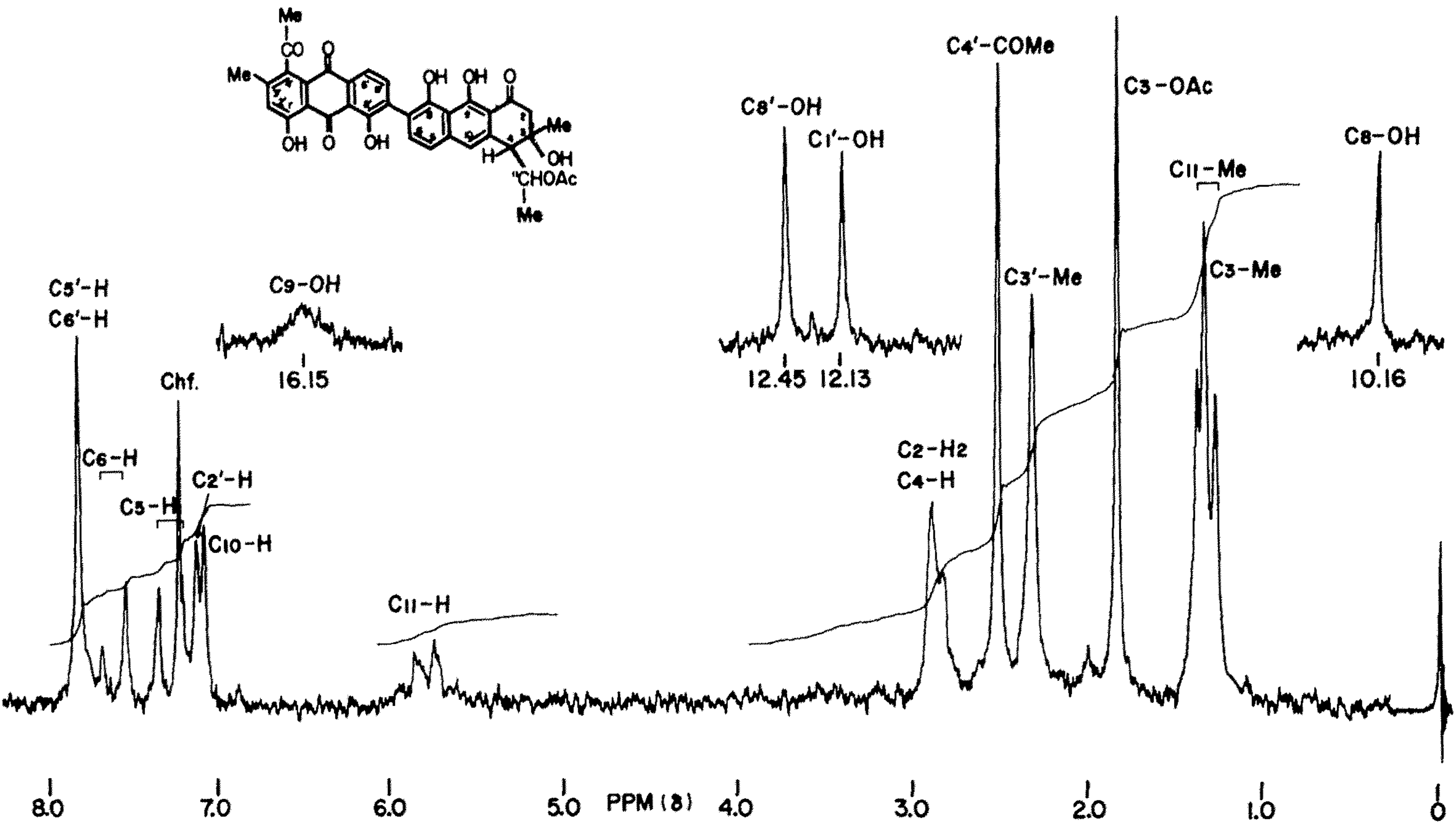
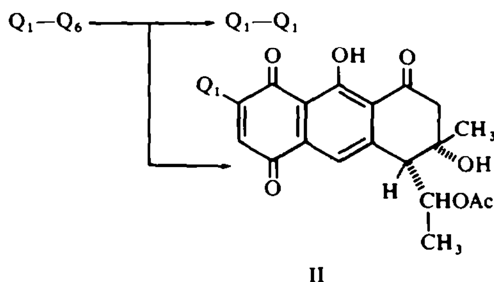


FIG 3. NMR spectrum of IV

Since its R_f value on acidic silica gel is slightly higher than those of julichromes $Q_{1\cdot5}$ and $Q_{1\cdot2}$, the structure was predicted as Q_5—Q_6 or Q_2—Q_6. The presence of a Q_6 unit was also proposed by the TLC on silica gel G, because the R_f value on this plate was much lowered, as is characteristic of the Q_6 unit.

The NMR spectrum of IV clearly revealed the overlapping pattern of the signals assignable as Q_5 and Q_6 units (*cf* Fig 3), and confirmed its structure as Q_5—Q_6.



II

According to the acetate-malonate theory, the Q_6 unit, which lacks the O-function at C_{10} as does chromomycinone (V)[5] or flavomannin (VI),[6] should be the one initially synthesized and then oxidized at C_{10} to a quinone system such as the Q_1 unit. Therefore, the isolation of I and III together with julimycin B-II from julimycin B-complex gives proof of the biogenetic route to a quinone system.

EXPERIMENTAL

Julichrome $Q_{1\cdot6}$ (I). The sample recrystallized from AcOEt gave the following analytical data. (Found: C, 64·85; H, 5·06. $C_{38}H_{36}O_{13}$ requires: C, 65·14; H, 5·18%). From $CHCl_3$ it was obtained as a solvate. (Found: C, 50·23; H, 4·41; Cl, 19·60. $C_{38}H_{36}O_{13}\cdot H_2O\cdot 2CHCl_3$ requires: C, 50·17; H, 4·21; Cl, 22·22%); IR ν_{max} (Nujol) cm^{-1}: 3390–3440 (OH), 1740 (OAc), 1708) (CO), 1665 (non-chelated quinone CO), 1620–1630 (chelated CO); UV λ_{max} (MeOH) mμ (log ε): 231 (4·63), 272 (4·62), 420 (4·09); CD: $[\theta]_{410}$ 0, $[\theta]_{395}$ +6800, $[\theta]_{372-320}$ 0, $[\theta]_{304}$ −14,700, $[\theta]_{242}$ 0, $[\theta]_{231}$ −84,700, $[\theta]_{222}$ 0 (*c* 1·024 mg/2 ml MeOH).

The oxidation of I *with Fremy's salt.* To a soln of I (20 mg) in MeOH (10 ml) was added a soln of potassium nitrosodisulfonate (25 mg) in H_2O (10 ml), and the mixture was stirred at room temp for 3 hr. The MeOH was distilled off *in vacuo* and the residue was extracted with AcOEt to give 19 mg crude amorphous powder. The products were separated by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 96:4). The upper brown zone gave 8 mg material which was mainly recovered I. The bottom yellow zone gave 10 mg crude II. The material from the upper zone was dissolved in 10 ml MeOH and further treated with a soln of potassium nitrosodisulfonate (10 mg) for 4 hr. Working up as above gave 4 mg of a I containing mixture and 5 mg of II. The former mixture was separated twice by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 98·5:1·5 for 17 hr) to afford 3 mg I and about 0·5 mg julimycin B-II in a pure state. Julimycin B-II obtained by this procedure was identified with an authentic sample by continuous development TLC on acidic silica gel, colour reaction with $Mg(OAc)_2$, and by comparison of R_f values on neutral silica gel G.

The crude II was combined and reseparated by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 96:4) to give 13 mg II. Recrystallization from MeOH gave orange prisms, m.p. >280°. (Found: C, 62·24; H, 4·76. $C_{38}H_{34}O_{14}\cdot H_2O$ requires: C, 62·29; H, 4·95%); IR ν_{max} (Nujol) cm^{-1}: 3628 (w), 3493, 3435 (OH), 1745, 1736 (OAc), 1710 (CO), 1667 (non-chelated quinone CO), 1635 (w) (chelated quinone CO). UV λ_{max} (MeOH) mμ (log ε): 232 (4·75), 280 (sh) (4·29), 430 (4·10). The oxidation of I with $K_2Cr_2O_7$ in AcOH at 100° gave similar results.

Julichrome $Q_{6\cdot6}$ (III). III, recrystallized from benzene showed the following properties. (Found: C, 66·61; H, 5·66. $C_{38}H_{38}O_{12}$ requires: C, 66·46; H, 5·58%); IR ν_{max} (Nujol) cm^{-1}: 3500, 3375 (OH), 1720 (OAc),

1600–1625 (s) (chelated CO and aromatic ring); UV λ_{max} (MeOH) mμ (log ε): 231 (4·64), 268 (sh) (4·71), 278 (4·80), 426 (4·38); CD: $[\theta]_{350}$ 0, $[\theta]_{304}$ −26,700, $[\theta]_{298}$ −19,300, $[\theta]_{280}$ −74,000, $[\theta]_{265}$ 0, $[\theta]_{254}$ +55,400, $[\theta]_{238}$ 0, $[\theta]_{228}$ −54,690, $[\theta]_{219}$ 0 (*c* 1·699 mg/ml, MeOH).

Julichrome $Q_{5\cdot6}$ (IV). This pigment has been reported as an amorphous powder, but later it was crystallized from MeOH as red prisms, m.p. 190–198°. (Found: C, 65·86; H, 5·09. $C_{38}H_{30}O_{11} \cdot H_2O$ requires: C, 65·85; H, 4·91%); IR ν_{max} ($CHCl_3$) cm^{-1}: 3623 (w), 3370 (OH), 1740 (OAc), 1700 (φ-CO), 1668 (m) (non-chelated quinone CO), 1626 (s) (chelated CO); UV λ_{max} (MeOH) mμ (log ε): 231 (4·62), 268 (4·68), 435 (4·29) CD: $[\theta]_{300}$ 0, $[\theta]_{260}$ +15,900, $[\theta]_{237}$ 0 (*c* 0·661 mg/5 ml, MeOH).

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