*Tetrahedron*. Vol. 26, pp. 5719 to 5729 Pergamon Press 1970. Printed in Great Britain

# STUDIES ON JULIMYCINS—VI

## THE STRUCTURES OF JULICHROMES $Q_{1\cdot2}$, $Q_{2\cdot2}$, $Q_{1\cdot5}$, $Q_{3\cdot5}$, $Q_{4\cdot5}$, $Q_{2\cdot5}$ AND $Q_{5\cdot5}$

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(*Received in Japan* 16 *May* 1970; *Received in the UK for publication* 29 *July* 1970)

**Abstract**—Julichromes $Q_{1\cdot2}$ and $Q_{2\cdot2}$ are identified as the dehydration products of julimycin B–II. The structures of julichromes, which commonly have a new anthraquinonyl $Q_5$ unit, are confirmed by their preparation from known julichromes. The conversion reaction, $Q_2 \rightarrow Q_5$, which involves an intra-molecular redox is probably concerned in the biosynthesis of this unit.

IN THE preceding paper,[1] the general method of isolation of julichromes, coloured metabolites of *Streptomyces shiodaensis*, was reported. The present paper is concerned with the pigments from the B-O and B-I fractions, which contain the pigments having comparatively large $R_f$-values (*cf* Fig 1). Among them, julichromes $Q_{2\cdot3}$ and $Q_{1\cdot4}$ have been established[2, 3] as $Q_2$—$Q_3$ and $Q_1$—$Q_4$ (*cf* Chart 1), respectively, and julichrome $Q_{5\cdot6}$ will be reported in the following paper together with julichromes $Q_{1\cdot6}$ and $Q_{6\cdot6}$. The remaining seven components of these fractions are detailed in this report.

Julichromes $Q_{1\cdot2}$ (I) and $Q_{2\cdot2}$ were readily shown to be anhydrojulimycin B-II ($Q_1$—$Q_2$)[4] and bisanhydrojulimycin B-II ($Q_2$—$Q_2$),[5] respectively, by continuous development TLC[1] and colour reaction with magnesium acetate. The structures were confirmed by comparison of the IR spectra with those of authentic samples.

Julichrome $Q_{1\cdot5}$ (III), $C_{36}H_{28}O_{12}$, is the main component of the B-I fraction and has been isolated as julimycin B-I[6] for the first time. The UV and IR spectra of III are very close to those of I and the NMR spectrum* clearly shows that III includes the known $Q_1$ unit in its molecule (*cf* Fig 2) as I. Accordingly, the unknown part of the molecule, the $Q_5$ unit ($C_{17}H_{11}O_5$), should be similar to the $Q_2$ unit and may be a derivative of 1,8-dihydroxyanthraquinone.

As shown in Fig 2, the $Q_5$ unit has two peri OH protons (12·47 ppm, 12·06 ppm), two aromatic protons (7·80 ppm), one additional aromatic proton (7·18 ppm) and one aromatic Me group (2·33 ppm). The latter aromatic hydrogen is probably located *ortho* to the aromatic Me group because of the broad shape of the two signals. These observations correspond to those of the $Q_2$ unit. Distinct from the $Q_2$ unit, however, the $Q_5$ unit has no signals attributable to a $\phi$-CH(OAc)-$CH_3$ group in its NMR spectrum, but has a sharp singlet (3H) at 2·52 ppm, which is assignable as a $\phi$-$COCH_3$ group. With respect to the biogenesis it is assumed that the $Q_5$ unit differs from the $Q_2$ unit only in the substituent at $C_4$ and that the structure of III could be indicated as $Q_1$—$Q_5$ (*cf* Chart 1). The confirmation of the structure is described below.

* NMR spectra were taken on a Varian A-60 spectrometer in $CDCl_3$ solution. Chemical shifts are expressed in $\delta$ (ppm) downfield from TMS used as internal reference.

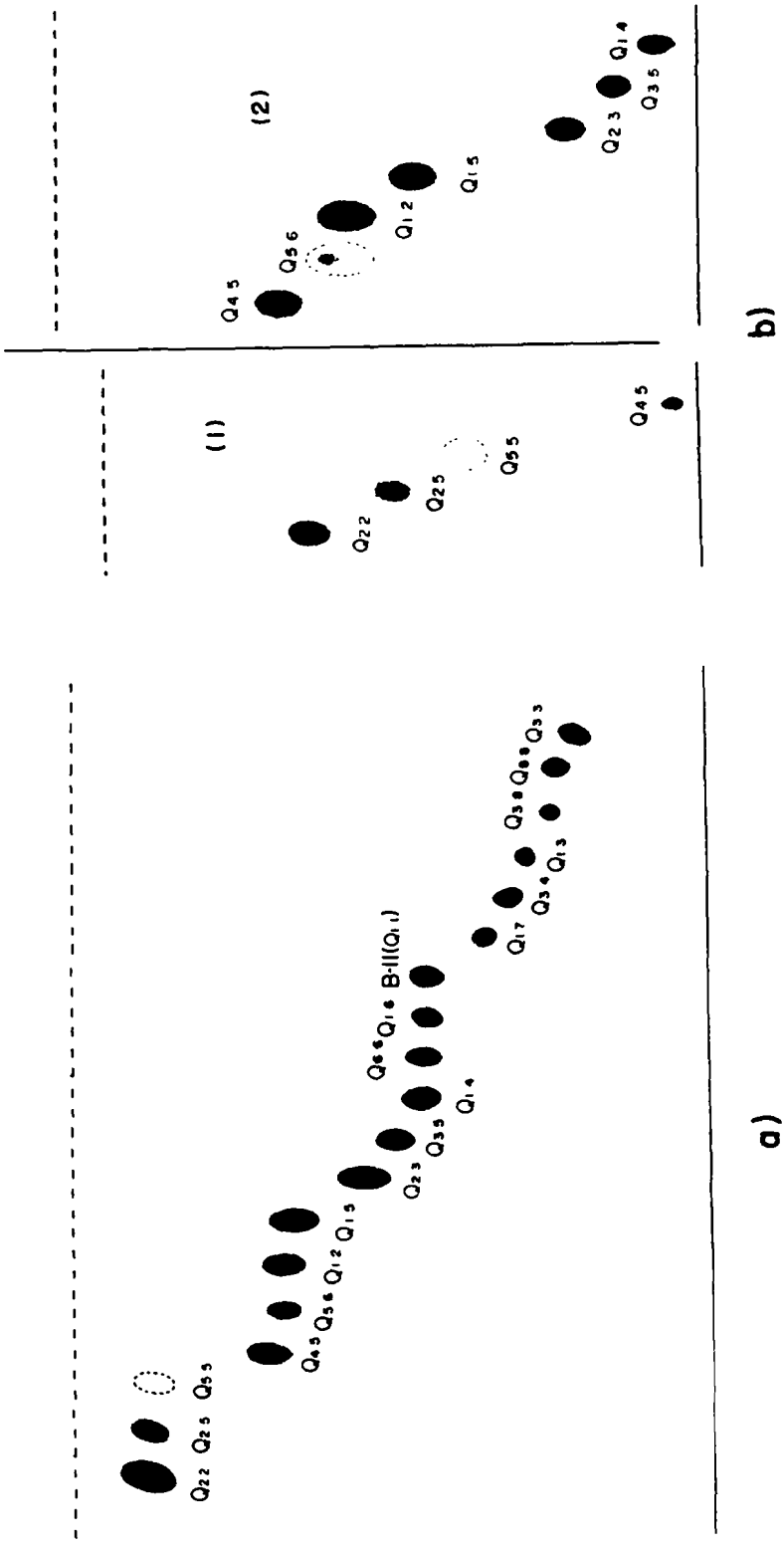


FIG 1. TLC of julichromes on acidic silica gel
(a) Ordinary TLC ($CHCl_3$–MeOH, 9:1)
(b) Continuous development TLC
(1) B–O fraction ($CHCl_3$–MeOH, 99:1, 1 hr)
(2) B–1 fraction ($CHCl_3$–MeOH, 98:2, 4·5 hr)

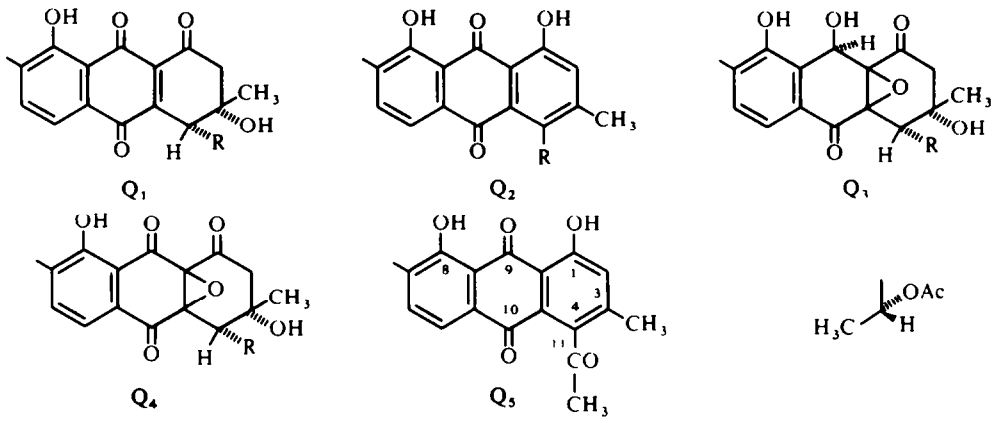

CHART 1

Julichrome $Q_{3\cdot5}$ (IV) has the molecular formula, $C_{36}H_{30}O_{13}$, and is stable in pyridine solution. Since IV gave a trimethoxy derivative on treatment with methyl iodide and silver oxide, the presence of three phenolic OH groups in the molecule is indicated. The NMR spectrum of the trimethyl ether (*cf* Fig 3), in comparison with that of trimethyljulichrome $Q_{2\cdot3}$,[2] suggests that IV is composed of $Q_5$ and the known $Q_3$ unit (cf Chart 1).

Based on this suggestion the conversion reactions,[2] $Q_3 \rightarrow Q_4 \rightarrow Q_1$, were attempted to correlate IV with III (*cf* Chart 2). The oxidation of IV with potassium bichromate gave a product which was identical with julichrome $Q_{4\cdot5}$ (V) isolated from the natural metabolites. The NMR spectrum of V clearly showed the overlapping signals of the known $Q_4$ unit and the $Q_5$ unit. On treatment with potassium iodide in acetic acid, V yielded III which was identical with the specimen isolated from the metabolites.

Next, the pigments in the B—O fraction are described. As reported previously,[1] the yield of this fraction is very low, which makes further investigation difficult. Fortunately, however, the TLC on acidic silicagel of the known pigments reveals a regular relationship between the $R_f$ values and structures, and this was useful for the presumption of the unknown julichromes. The contribution of the known units to the $R_f$ value is empirically estimated as being in the following order (*cf* Fig 1): $Q_2 > Q_5 \gg Q_4 > Q_1 \gg Q_3$.*

Since II has the structure $Q_2$—$Q_2$ as mentioned above, the other two pigments, julichromes $Q_{2\cdot5}$ (VI) and $Q_{5\cdot5}$ (VII) having similar $R_f$-values, would consist of two of such units as $Q_2$ or $Q_5$. If $Q_2$ and $Q_5$ units are the only constituent elements of these pigments, the structures of VI and VII should be shown as $Q_2$—$Q_5$ and $Q_5$—$Q_5$, respectively, on account of their $R_f$ values, II > VI > VII. In fact the dehydration of III in pyridine solution gave VI in a good yield, thus supporting the structure of VI.

On the other hand, though the structure of VII ($Q_5$—$Q_5$) is likely from the elemental analysis and IR spectrum, which lacks the absorption band of acetoxyl function, unequivocal proof by the correlation of VII to a known julichrome was desirable. The

* $\gg$ can be distinguished by ordinary TLC
$>$ can be distinguished by continuous development TLC

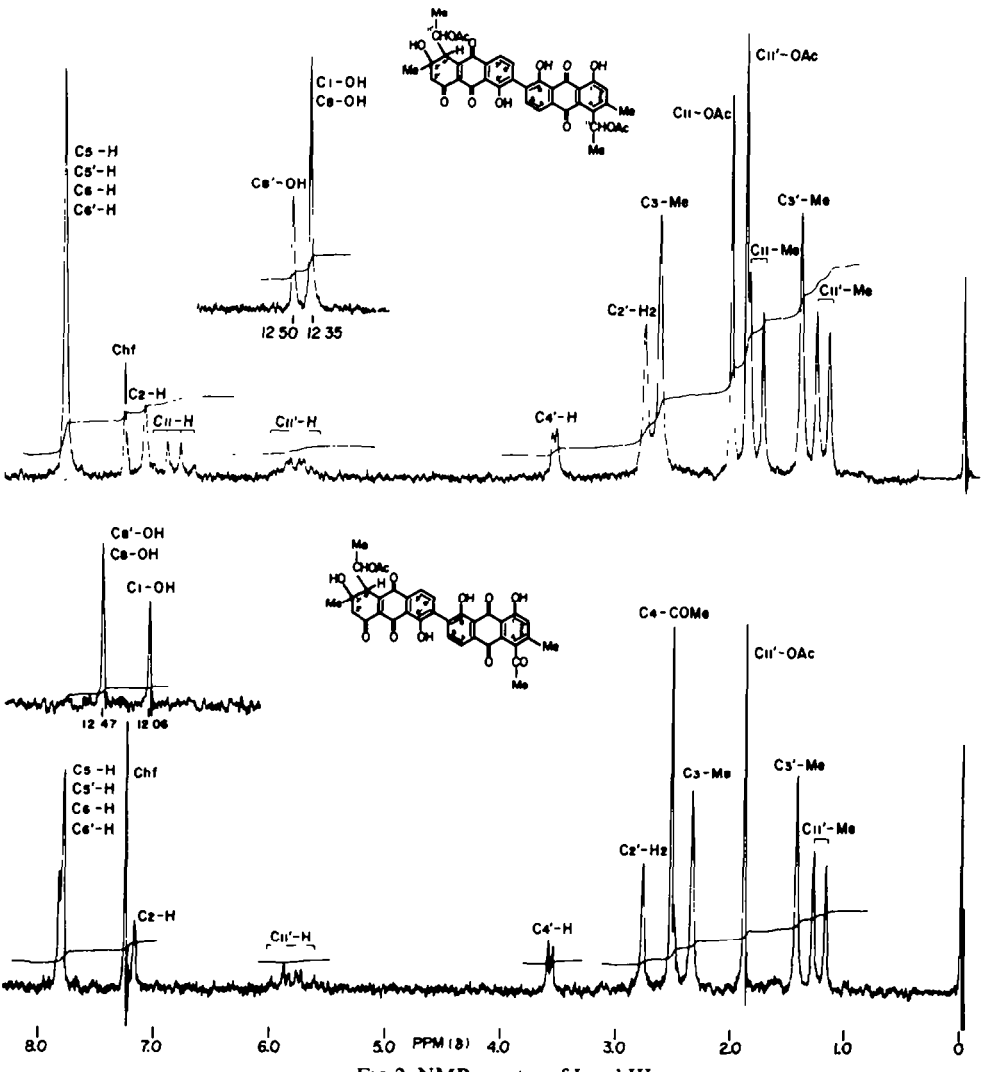


FIG 2. NMR spectra of I and III

attempt, deacetylation of II and subsequent oxidation of the deacetyl compound to VII, was unsatisfactory due to the difficulty of the oxidation step. Unexpectedly, however, it was found that II was easily converted to VII on heating with *p*-toluenesulfonic acid in aqueous DMSO, and VI was also isolated as an intermediate of this reaction. By the same reaction the tetramethyl ether of II gave in good yield a product identical with the methylation product of VII. The NMR spectrum of the tetramethyl ether of VII (*cf* Fig 4) clearly proves that VII consists of two $Q_5$ units.

This conversion reaction, $Q_2 \rightarrow Q_5$, confirmed not only the structure of VII but also those of the other above-mentioned pigments having $Q_5$ unit.

Nevertheless, the preparation of III from I by similar treatment failed. In this case, the $Q_1$ unit of I was dehydrated to a $Q_2$ unit before the desired conversion, and the products were identical with those from II. Similarly, julichrome $Q_{1\text{-}3}$ ($Q_1$—$Q_3$) as

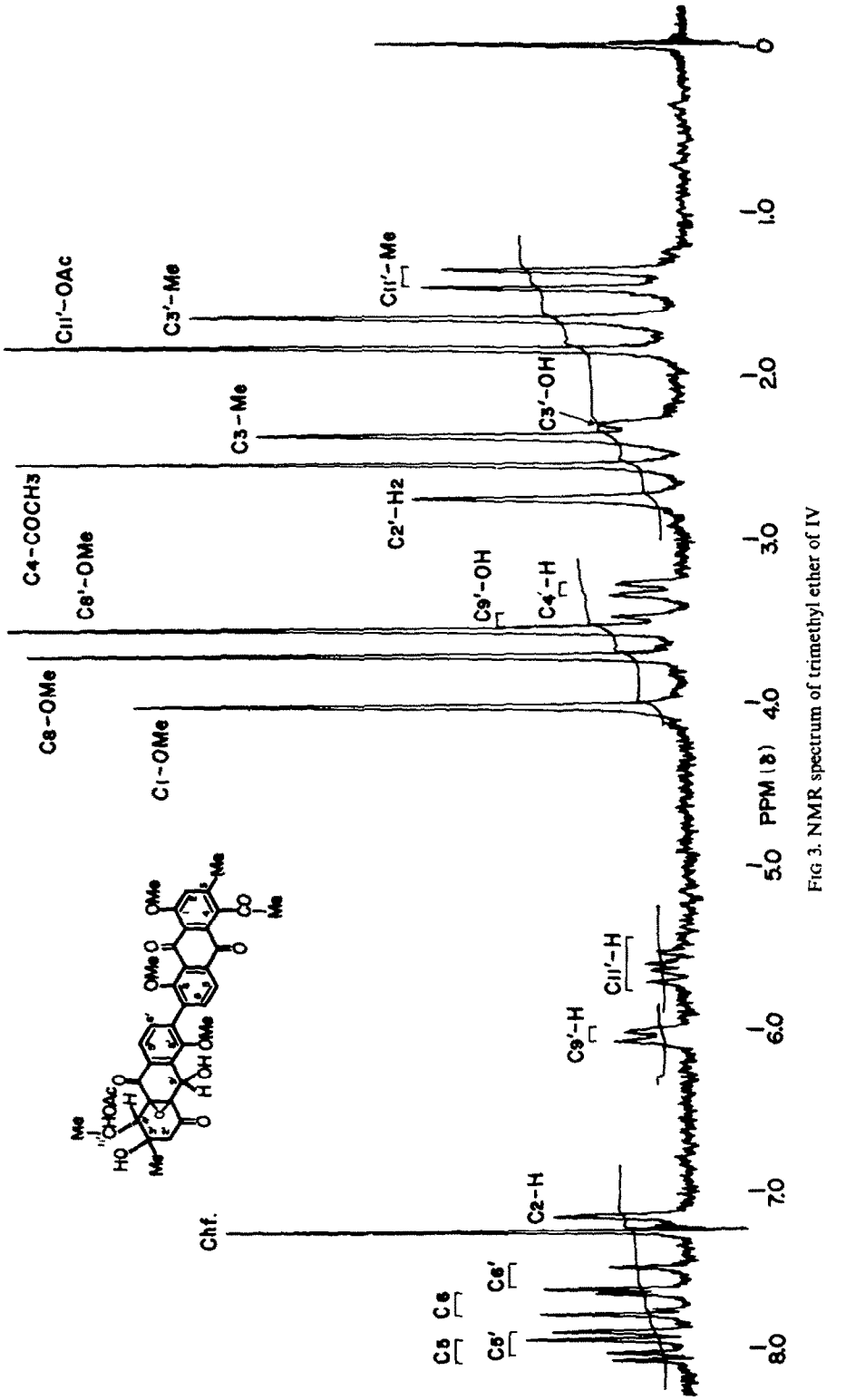


FIG 3. NMR spectrum of trimethyl ether of IV

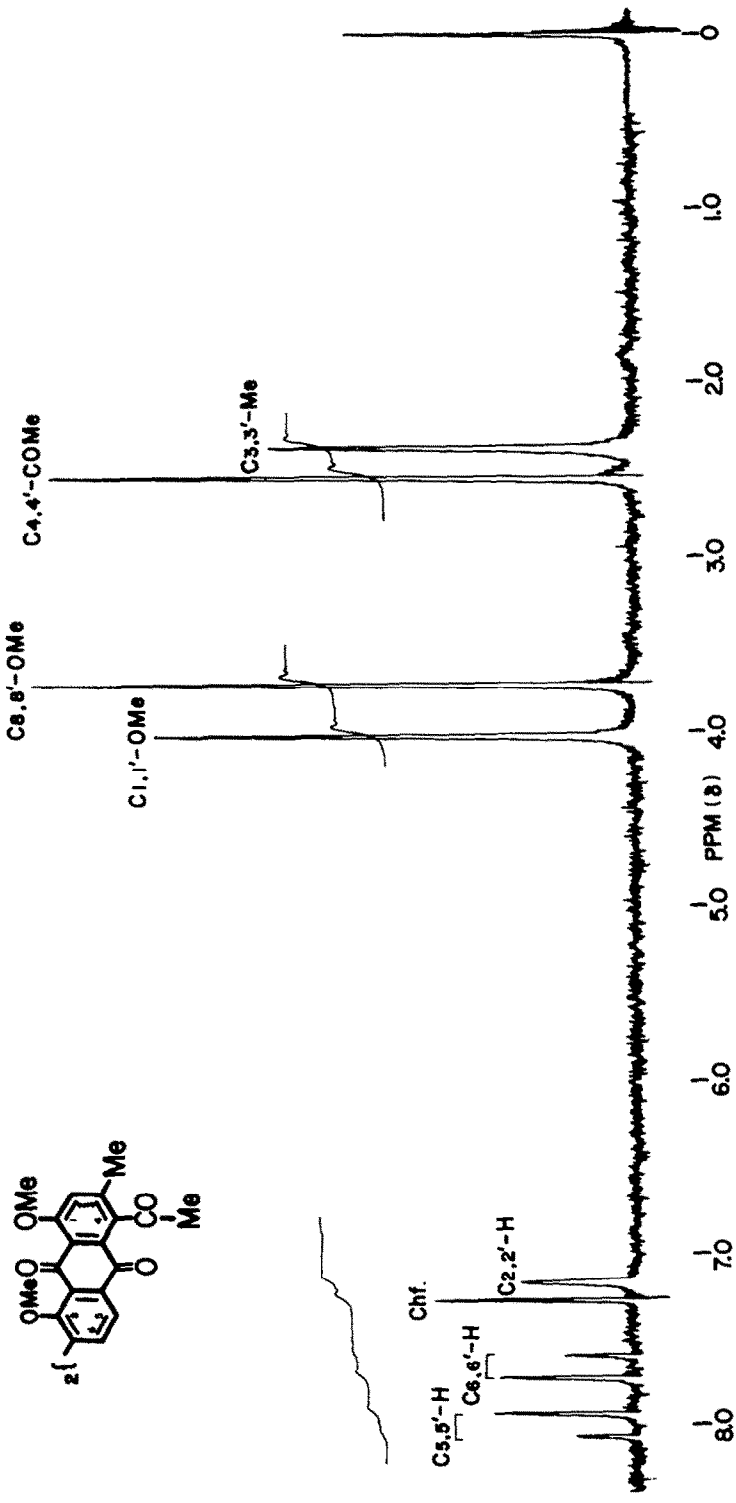


FIG 4. NMR spectrum of tetramethyl ether of VII

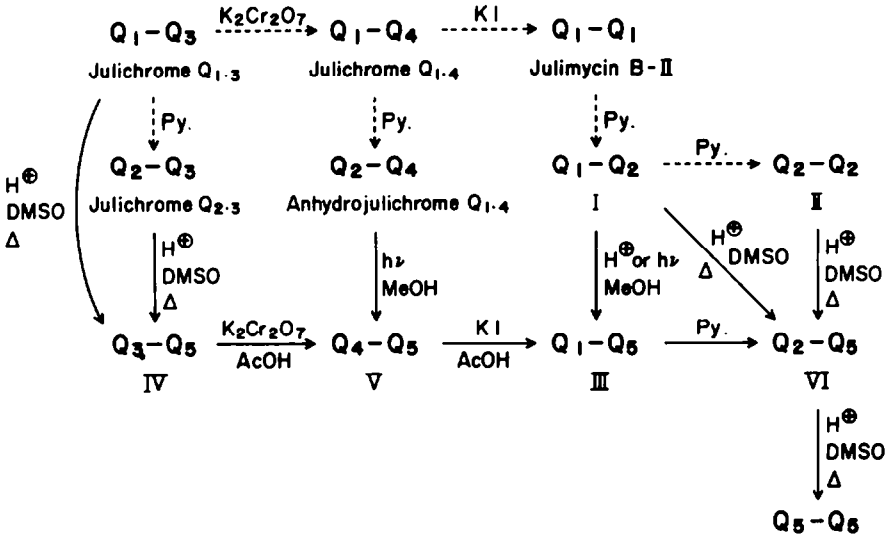


CHART 2*

well as $Q_{2\cdot3}$ ($Q_2$—$Q_3$) gave IV. While the light irradiation of a methanol solution of I without acid afforded III in fairly good yield. Further, standing the methanol solution of I with *p*-toluenesulfonic acid at room temperature also gave III even in a dark room.

As summarized in Chart 2, the preparation of these minor pigments from the known julichromes clearly confirms their stereochemistry.

Unfortunately, since the yields of II, V and VI from the natural metabolites were too low for the measurement of optical activities, the absolute stereochemistry could not be confirmed. However, it is in order to assume that the $Q_2$ and $Q_4$ units of these pigments have the same absolute configurations as those of other known pigments such as julichromes $Q_{2\cdot3}$ and $Q_{1\cdot4}$. Since the $Q_5$ unit lacks an asymmetric C atom, VII, which consists of two $Q_5$ units, shows no optical activity.†

As the conversion, $Q_2 \rightarrow Q_5$, is readily accomplished, it is interesting from the biogenetic point of view. Careful examination of this reaction by TLC demonstrated that I was converted to III *via* an intermediate (VIII) which has a lower $R_f$ value than I or III. Since VIII is very unstable and is easily changed into III in the air or by the action of silver oxide, it should be one of the two possible hydroquinones corresponding to III, though its isolation in a pure state was unsuccessful. With magnesium acetate the peri-hydroxyquinones change colour[7] while the corresponding hydroquinones are inert. Regarding the known julichromes, as summarized in Table 1, the pigments having a $Q_1$ unit turn a blue-tone and those having a $Q_5$ unit turn a red-tone. Since VIII turns pale green with this reagent, it is likely that the colour change is due to the $Q_1$ unit in the molecule. Moreover, julimycin B-II ($Q_1$—$Q_1$) is stable under light or acid. Therefore, VIII should be the hydroquinone which is hydrogenated at the $Q_5$

* The conversions shown in dotted lines have been reported previously.[2–5]

† The absence of restricted rotation about the biphenyl linking has been proved.[5]

TABLE 1. THE COLOUR REACTION WITH $Mg(oAc)_2$

| | |
|---|---|
| $Q_1-Q_1$ | blue |
| $Q_1-Q_3$ | violet |
| $Q_1-Q_2$ | purple |
| $Q_1-Q_5$ | purple |
| $Q_2-Q_5$ | deep red |
| $Q_5-Q_5$ | deep red |
| $Q_3-Q_5$ | red |

unit of III, and the conversion reaction could be explained by the pathway shown in Chart 3. The intramolecular hydrogen transfer from the benzylic carbon ($C_{11}$) to the quinone CO is reasonable from the sterically favoured arrangement of $C_{11}-H$ for a 6-membered transition state.

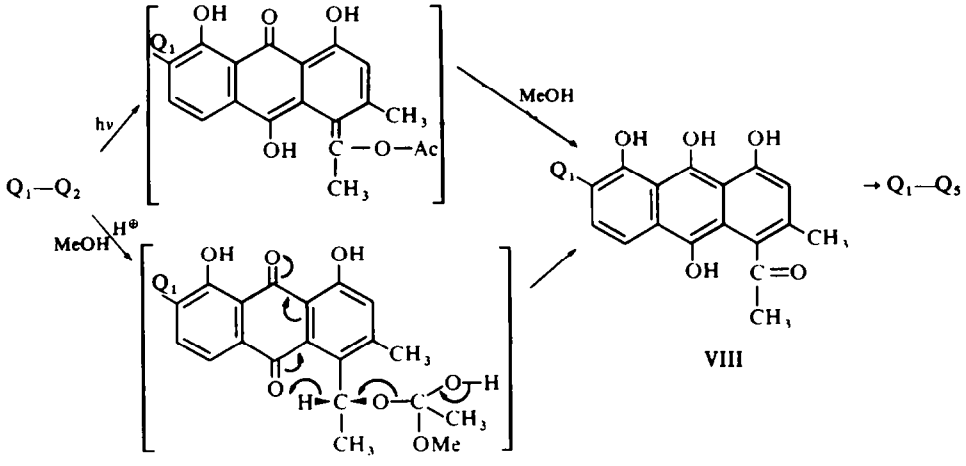


CHART 3

Since the conversion proceeds very easily, it is a delicate problem whether this type of reaction takes part in the biosynthesis or whether the $Q_5$ unit is an artifact in the isolation process. In the course of the precise separation of julimycin B-complex,[1] a considerable amount of III was isolated from the B-II fraction (below B-I fraction) which had been completely separated from the pigments of B-I fraction by column chromatography and successive preparative TLC. Similarly, V was isolated not only from the B-I fraction but also from the SV fraction (below the B-II fraction). It is difficult to attribute these results to the tailing of III or V on chromatography. Moreover, the amount of III in a fresh extract (ethyl acetate) of the fermentation broth was negligible on TLC, but after standing for a few days the extract gave a distinct spot of III. These facts suggest that III is not a direct product of the fermentation.

On the other hand, since the spot of I is also negligible in the fresh extract, I cannot be the direct precursor of III. Further, pure julimycin B-II did not show any remarkable change on standing in dry or water saturated ethyl acetate solution for two weeks* nor on chromatography using acidic adsorbants. These experiments preclude the occurrence of the transformation, $Q_1 \rightarrow Q_2 \rightarrow Q_5$, during isolation.

* The conversion, $Q_1 \rightarrow Q_5$, was observed on standing for 5 months in dry solution.

Accordingly, the most reasonable precursor is a hydroquinone which has a lower $R_f$ value than III and which is easily convertible to III by air oxidation. Any one of the three hydroquinones, VIII ($Q_1$—dihydro $Q_5$), dihydro $Q_1$—$Q_5$ and dihydro $Q_1$—dihydro $Q_5$, is possible as a precursor, and the pigments having a dihydro $Q_1$ unit were actually isolated from the natural metabolites as reported later. However, the behaviour of III in the isolation process is common with the pigments having the $Q_5$ unit and in the case of IV and VII, for example, the structure of the hydroquinone cannot be any form other than the dihydro $Q_5$ unit. Therefore, VIII is the most probable precursor of III, though its isolation could not be achieved because of its instability and the presence of many other pigments in the B-II fraction. Thus, it may be concluded that the final step in the formation of the $Q_5$ unit might be attributed to air oxidation, but the dihydro $Q_5$ unit at least is produced in the fermentation process from a $Q_2$ unit by way of a reaction such as that described.

## EXPERIMENTAL*

*Julichrome* $Q_{1\cdot2}$ (I)

This pigment was identical with monoanhydrojulimycin B-II in all respects; IR $\nu_{max}$ ($CHCl_3$) $cm^{-1}$: 3400–3580 (w.) (OH), 2600–3200 (broad) (chelated OH), 1737 (OAc), 1705 (6-membered ring CO), 1668 (non-chelated quinone CO), 1627 (chelated quinone CO); UV $\lambda_{max}$ ($CHCl_3$) mμ (log ε): 266 (4·60), 460 (4·27); CD: $[\theta]_{330}$ 0, $[\theta]_{299}$ +11,200, $[\theta]_{286}$ 0, $[\theta]_{258}$ −42,800 (*c*, 1·009 mg/5 ml, $CHCl_3$).

*Julichrome* $Q_{2\cdot2}$ (II)

Since the yield of II was very poor, it was identified with authentic bisanhydrojulimycin B-II by continuous development TLC and by comparison of IR spectra; IR $\nu_{max}$ ($CHCl_3$) $cm^{-1}$: 2400–3300 (broad) (chelated OH), 1730 (OAc), 1670 (non-chelated quinone CO), 1628 (chelated quinone CO).

*Julichrome* $Q_{1\cdot5}$ (III)

The compound showed the following analytical data. (Found: C, 66·54; H, 4·50. $C_{36}H_{28}O_{12}$ requires: C, 66·25; H, 4·32%); IR $\nu_{max}$ ($CHCl_3$) $cm^{-1}$: 3593 (w.) 3400–3500 (w.) (OH), 2600–3200 (chelated OH), 1740 (m.) (OAc), 1706 (broad) (6-membered ring CO and $\phi$-$COCH_3$), 1670 (non-chelated quinone CO), 1630 (chelated quinone CO); UV $\lambda_{max}$ ($CHCl_3$) mμ (log ε): 265 (4·59), 460 (4·30); CD: $[\theta]_{290}$ 0, $[\theta]_{260}$ −17,100, $[\theta]_{228}$ 0, $[\theta]_{215}$ +15,800 (*c*, 1·024 mg/5 ml, MeOH).

*Julichrome* $Q_{3\cdot5}$ (IV)

Compound IV was recrystallized from MeOH containing ½ mole $H_2O$. (Found: C, 63·50; H, 4·59. $C_{36}H_{30}O_{13}\cdot\frac{1}{2}H_2O$ requires: C, 63·62; H, 4·60%). A dried sample (at 120°, 2 mm Hg) gave the following data: (Found: C, 64·07; H, 4·59. $C_{36}H_{30}O_{13}$ requires: C, 64·47; H, 4·51%); IR $\nu_{max}$ (Nujol) $cm^{-1}$: 3524 (OH), 1725–1695 (OAc, CO), 1666 (w.) (non-chelated quinone CO), 1627 (chelated quinone CO); UV $\lambda_{max}$ (MeOH) mμ (log ε): 229 (4·54), 265 (4·48), 444 (4·07); CD: $[\theta]_{375}$ 0, $[\theta]_{335}$ +24,000, $[\theta]_{303}$ 0, $[\theta]_{275}$ −11,200, $[\theta]_{243}$ 0. (*c*, 1·500 mg/5 ml MeOH).

*Methylation of* IV

A soln of IV (50 mg) in acetone (10 ml) was refluxed with MeI (3 ml) and $Ag_2O$ (prepared from 425 mg $AgNO_3$) under stirring. After 1·5 hr the mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by preparative TLC on silica gel G ($CHCl_3$—MeOH, 9:1). The material (36 mg) from the main zone was recrystallized from MeOH to give the trimethyl ether of IV as yellow needles, m.p. 245–247°. (Found: C, 65·77; H, 5·21; MeO, 12·60. $C_{39}H_{36}O_{13}$ requires: C, 65·72; H, 5·09; MeO, 13·06%).

*Oxidation of* IV *to julichrome* $Q_{4\cdot5}$ (V)

To a hot soln of IV (20 mg) in AcOH (1·5 ml), a soln of $K_2Cr_2O_7$ (4·5 mg) in AcOH (0·5 ml) was added at 100° during 5 min. After an additional 10 min the soln was poured into $H_2O$ and extracted with $CHCl_3$.

* M.ps were determined on a hot plate and are not corrected.

The $CHCl_3$ layer was washed 4 times with $H_2O$, dried over $MgSO_4$ and evaporated to give 20 mg red syrup, which was separated by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 98:2) to afford 9 mg of product (from the upper zone) and 6 mg of starting material (from the bottom zone). The main product was recrystallized from MeOH to give V as orange prisms, m.p. 241–246°. (Found: C, 64·37; H, 4·37. $C_{36}H_{28}O_{13}$ requires: C, 64·67; H, 4·22%); IR $\nu_{max}$ (Nujol) $cm^{-1}$: 3560 (w.), 3400 (OH), 1724 (OAc), 1702 (CO), 1665 (non-chelated quinone CO), 1625 (chelated quinone CO); UV $\lambda_{max}$ (MeOH) mμ (log ε): 229 (4·60), 262 (4·63), 439 (4·25).

The IR spectrum of this substance was identical with that of julichrome $Q_{4\cdot5}$ (V) isolated from the natural metabolites.

*Conversion of* V *to* III

A mixture of 5 mg V and KI (30 mg) in AcOH (1 ml) was stirred at room temp for 30 min. The solvent was distilled off *in vacuo* and the residue was purified by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 98:2). The substance (5 mg) from the main red zone was recrystallized from acetone to yield 2·5 mg of III, which had an IR spectrum identical with that of sample isolated from the metabolites.

*Dehydration of* III *to julichrome* $Q_{2\cdot5}$ (VI)

A soln of III (30 mg) in pyridine (1 ml) was heated on a steam bath for 2 hr. The pyridine was distilled off and the residue was purified by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 95:5). Recrystallization ($CHCl_3$—MeOH) of the substance from the main zone gave 24 mg of VI as red prisms, m.p. >300°. (Found: C, 68·31; H, 4·07. $C_{36}H_{26}O_{11}$ requires: C, 68·13; H, 4·13%); IR $\nu_{max}$ (Nujol) $cm^{-1}$: 1740 (OAc), 1703 ($\phi$—CO—$CH_3$), 1670 (non-chelated quinone CO), 1630 (chelated quinone (CO); UV $\lambda_{max}$ ($CHCl_3$) mμ (log ε): 268 (4·70), 292 (sh.) (4·34), 462 (4·49).

*Julichrome* $Q_{5\cdot5}$ (VII)

VII, m.p. > 300°, is sparingly soluble in most organic solvents. (Found: C, 68·87; H, 3·88. $C_{34}H_{22}O_{10}$ requires: C, 69·15; H, 3·76%); IR $\nu_{max}$ (Nujol) $cm^{-1}$: 1697 ($\phi$-$COCH_3$), 1669 (non-chelated quinone CO), 1626 (chelated quinone CO); UV $\lambda_{max}$ ($CHCl_3$) mμ (log ε): 266·5 (4·72), 292 (sh.) (4·36), 464 (4·46).

*Conversion of* II *to* VI *and* VII *in DMSO*

A mixture of II (44 mg), *p*-TsOH (44 mg) and $H_2O$ (2 ml) in DMSO (20 ml) was heated at 100° for 40 hr. The reaction mixture was poured into $H_2O$ and extracted with $CHCl_3$. The residue from the extract was separated by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 98·5:1·5). The substance (6 mg) from the first main zone was starting material. The second zone gave 14 mg of yellow pigment, which was recrystallized from MeOH to afford 12 mg VI, identical with an authentic specimen. The third zone gave 6 mg of VII, which was identified by IR spectrum with the pigment isolated from the natural metabolites. This product as well as natural specimen is optically inactive.

*Tetramethyl ethers of* VI *and* VII *from tetramethyljulichrome* $Q_{2\cdot2}$[4]

To a suspension of tetramethyl ether of II (70 mg in DMSO (30 ml), a soln of *p*-TsOH (70 mg) in $H_2O$ (1 ml) was added and the mixture was heated at 100° for 90 hr. During the period the mixture gradually became a complete soln. The reaction mixture was treated as above. Continuous development TLC on the same adsorbant ($CHCl_3$—MeOH, 98:2) gave two main yellow zones. The substance (9 mg) from the upper zone was identical with the methyl ether of VI prepared by the treatment of VI with MeI—$Ag_2O$ in acetone.

The bottom zone of the TLC gave 55 mg of coloured material, which was solidified with ether to a yellow powder. (Found: C, 70·32; H, 4·88. $C_{38}H_{30}O_{10}$ requires: C, 70·58; H, 4·68%).

This compound had an IR spectrum identical with that of the methylation product of VII.

*Compound* IV *from julichrome* $Q_{1\cdot3}$

A mixture of julichrome $Q_{1\cdot3}$ (20 mg), *p*-TsOH (20 mg), $H_2O$ (2 ml) and DMSO (10 ml) was heated at 85° for 74 hr. Working up as above gave 7·5 mg julichrome $Q_{2\cdot3}$ and 12 mg of IV, which was identical with the sample isolated from the natural metabolites.

By the same treatment, julichrome $Q_{2\cdot3}$ also gave IV.

*Conversion of* I *to* III

(i) *By light irradiation.* A soln of I (9 mg) in MeOH (10 ml) was irradiated at 10° with a 300-Watt high-pressure mercury lamp combined with a glass filter to eliminate wave-lengths below 5600 Å. After 4 hr the solvent was distilled off and the residue was fractionated by continuous development TLC on acidic silica gel ($CHCl_3$—MeOH, 97·5:2·5). From the first red zone 2 mg of I was recovered, and the second red zone gave 3 mg of III which was identical with a natural specimen. The yellow zones below III afforded 5 mg of crude hydroquinone VIII, which was oxidized with $Ag_2O$ in acetone for 20 min at room temp. Purification of the product by TLC as above gave 2 mg of III.

(ii) *By acid-catalysed conversion.* To a soln of I (10 mg) in MeOH (7 ml) was added *p*-TsOH (10 mg), and the mixture was allowed to stand for 48 hr in a dark room. The TLC of the mixture showed spots corresponding to III, I and VIII. The solvent of the reaction mixture was distilled off *in vacuo* and the residue was treated with $CHCl_3$ and $H_2O$. The $CHCl_3$ layer was washed with $H_2O$, dried over $MgSO_4$ and evaporated. The residue was treated with $Ag_2O$ in acetone for 30 min. The spot of VIII disappeared on this treatment. Working up as usual gave 2 mg III and 6 mg of recovered I.

*Compound* V *from anhydrojulichrome* $Q_{1\,4}$[2]

A soln of anhydrojulichrome $Q_{1\,4}$ (9 mg dioxan (0·5 ml) and MeOH (10 ml) was irradiated as above for 2 hr. The mixture was treated with $Ag_2O$, and the product was separated by continuous development TLC ($CHCl_3$—MeOH, 98:2) to give 2 mg V, which was identified with an authentic sample by IR spectrum.

*Acknowledgement*—The authors are indebted to Drs. K. Takeda and Y. K. Sawa of this laboratory for their interest.

## REFERENCES

[1] N. Tsuji, K. Nagashima, T. Kimura and H. Kyotani, *Tetrahedron* **25**, 2999 (1969).
[2] N. Tsuji and K. Nagashima, *Ibid.* **25**, 3007 (1969)
[3] N. Tsuji and K. Nagashima, *Ibid.* **25**, 3017 (1969)
[4] N. Tsuji, *Ibid.* **24**, 1765 (1968)
[5] N. Tsuji and K. Nagashima, *Ibid.* **24**, 4233 (1968)
[6] J. Shoji, Y. Kimura and K. Katagiri, *J. Antibiotics, Ser. A*, **17**, 156 (1964)
[7] S. Shibata, *Yakugaku Zasshi* **61**, 320 (1941)