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THE REACTIONS OF CHROMOMYCINONE AND DERIVATIVES

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Abstract—The various reactions of chromomycinone, the chromophore of the cancerostatic chromomycins, are described. The structures of several chromomycinone derivatives are also discussed.

Chromomycinone (CHR) (1)

CHROMOMYCIN A_3[1] could be hydrolysed either with aqueous acetic acid at 80° or with methanolic hydrogen chloride at room temperature to give the four chromoses[2] and the chromophore designated chromomycinone[3] (abbreviated to CHR); a higher yield of CHR was obtained by the latter method. During the early stages of investigation, the isolation of crystalline CHR proved to be troublesome and had to be carried out by chromatography on silica gel containing 1% oxalic acid. However, it was later found that concentration of an acetic acid solution of CHR afforded yellow crystals of CHR containing 2 moles of acetic acid; the solvent of crystallization could then be removed by heating the crystals *in vacuo* at 100° to give crystalline CHR.

Since the derivation of structure **1** for CHR, which depended heavily on NMR, especially decoupling and solvent shift techniques, has already been presented in a previous communication[3] the present paper will be limited to a discussion of the reactions of CHR and its derivatives.

The close similarity of the UV spectra of chromomycin A_3 and CHR (Fig. 1) clearly indicate that CHR comprises the chromophore of the antibiotic, and moreover the two spectra are reminiscent of the tetracycline type spectrum, e.g., anhydroterramycin[4] and 1-keto-8,9-dihydroxy-1,2,3,4-tetrahydroanthracene (**2**) (Fig. 1). The model compound **2** was synthesized by reduction of chrysazin (**3**) with red phosphorus and hydroiodic acid to chrysanthrone (**4**)[5] followed by further reduction of the latter with platinum and hydrogen.

[1] M. Miyamoto, K. Morita, Y. Kawamatsu, M. Sasai, A. Nohara, K. Tanaka, S. Tatsuoka, K. Nakanishi, Y. Nakadaira and N. S. Bhacca, *Tetrahedron Letters* 2367 (1964); M. Miyamoto, Y. Kawamatsu, K. Kawashima, M. Shinohara and K. Nakanishi, *Tetrahedron Letters* 545 (1966).

[2] M. Miyamoto, Y. Kawamatsu, M. Shinohara, K. Nakanishi, Y. Nakadaira and N. S. Bhacca, *Tetrahedron Letters* 2371 (1964).

[3] M. Miyamoto, K. Morita, Y. Kawamatsu, S. Noguchi, R. Marumoto, K. Tanaka, S. Tatsuoka, K. Nakanishi, Y. Nakadaira and N. S. Bhacca, *Tetrahedron Letters* 2355 (1964).

[4] F. A. Hochstein, C. R. Stephens, L. H. Conover, P. P. Regna, R. Pasternack, P. N. Gordon, F. J. Pilgrim, K. J. Brunings and R. B. Woodward, *J. Amer. Chem. Soc.* **75**, 5455 (1953).

[5] H. Schrobsdorfe, *Chem. Ber.* **35**, 2930 (1962).

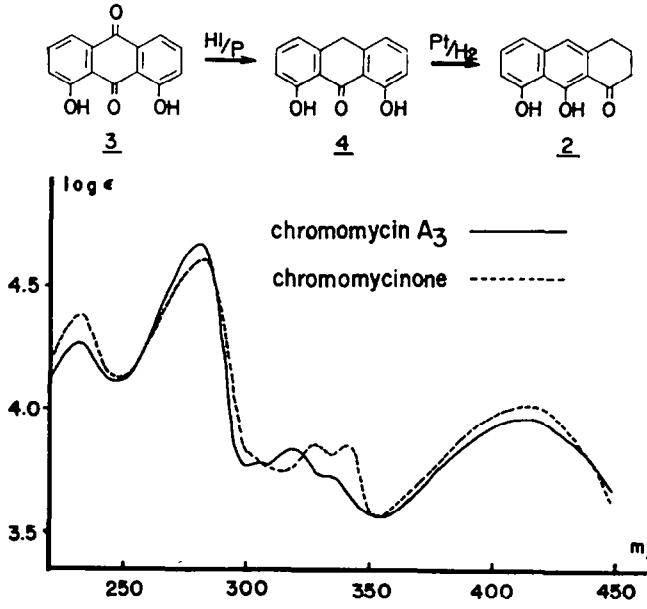


FIG. 1a. UV spectra of chromomycin A_3 and chromomycinone (1) in EtOH.

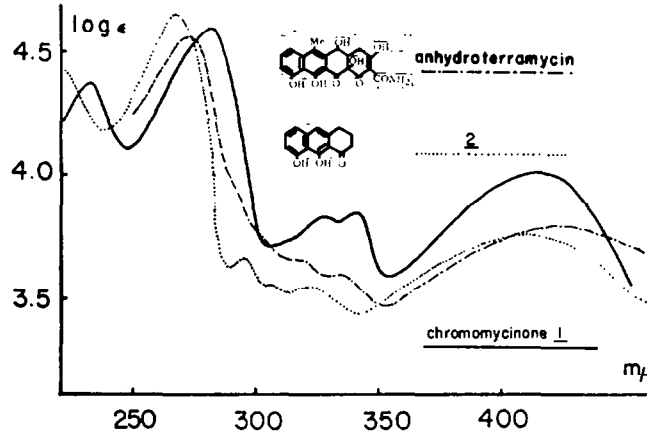


FIG. 1b. UV spectra of anhydroterramycin, 1-keto-8,9-dihydroxy-1,2,3,4-tetrahydroanthracene (2) and chromomycinone (1) in EtOH.

CHR *acetates*

When reacted with acetic anhydride containing a small amount of *p*-toluenesulfonic acid, CHR gave the acetates **5** and **6**, whereas with pyridine and acetic anhydride it gave the acetate **7**. The sites of the acetyl groups were determined on the basis of spectroscopic properties. Namely, a hypsochromic shift paralleling the degree of acetylation is noted in the UV maxima (Fig. 2), and since it is well-known[6] that acetylation of phenolic hydroxyls gives rise to a blue-shift in the UV absorption, this suggests that in addition to the three carbinol hydroxyls at C-2, C-3′ and C-4′,

[6] G. Just, W. C. Day and F. Blank, *Canad. J. Chem.* **41**, 74 (1963); A. J. Birch and F. W. Donovan, *Austral. J. Chem.* **6**, 360 (1953); A. J. Birch and F. W. Donovan, *Austral. J. Chem.* **8**, 529 (1955).

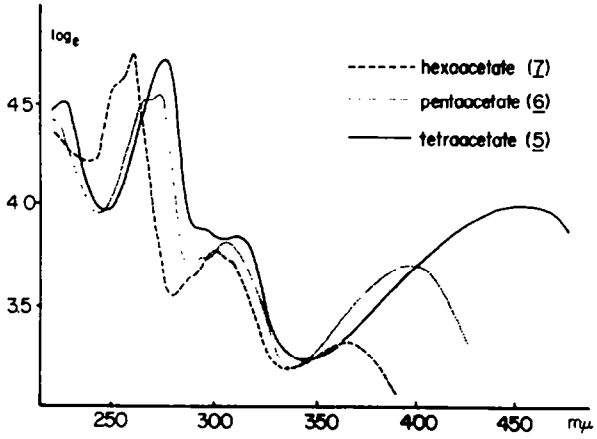
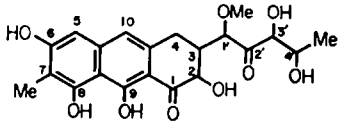


FIG. 2. UV spectra of chromomycinone tetraacetate (5), pentaacetate (6) and hexaacetate (7) in EtOH.



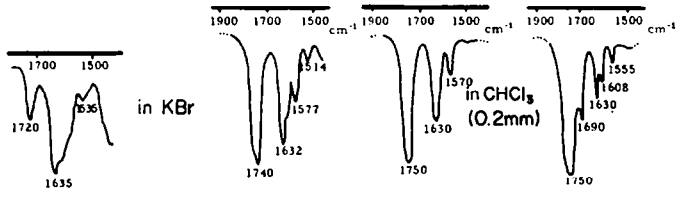
1

5 2, 6, 3′, 4′- tetraacetate

6 2, 6, 8, 3′, 4′- pentaacetate

7 2, 6, 8, 9, 3′, 4′-hexaacetate

the remaining three phenolic hydroxyls are successively acetylated. The NMR spectrum of the tetraacetate **5** still retained the two low-field signals at 9·72 and 15·20 ppm characteristic of the hydrogen-bonded 8-OH and 9-OH; thus it is the 6-OH that is acetylated. The pentaacetate **6** exhibited an NMR signal at 14·10 ppm, indicating the presence of one chelated hydroxyl; in conjunction with the appearance of the C_1-carbonyl IR band at 1630 cm^{-1} (Fig. 3c), a position indicative of chelation,[7] it is inferred that the 9-OH is left unacetylated. Finally, the hexaacetate shows an IR carbonyl band as expected at 1690 cm^{-1} (Fig. 3d), a position typical for aromatic carbonyls.



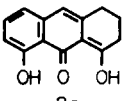
Chromomycinone (1) tetraacetate (5) pentaacetate (6) hexaacetate (7)

3a 3b 3c 3d

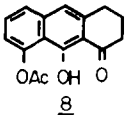
FIG. 3. IR spectra of chromomycinone (1), chromomycinone tetraacetate (5), pentaacetate (6) and hexaacetate (7).

[7] C. J. Covell, F. E. King and J. W. W. Morgan, *J. Chem. Soc.* 702 (1961); K. Nakanishi, *Infrared Absorption Spectroscopy—Practical.* Holden-Day (1964).

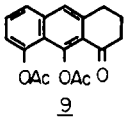
Two tautomeric modifications **2a** or **2b** are conceivable for the oxotetrahydroanthracene **2**, which was used as the UV model for CHR. A gradual hypsochromic shift is observed in the UV spectra in going from the free compound **2** to the monoacetate **8** and then to the diacetate **9** indicating that all three compounds have the



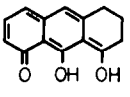
2a



8



9



2b

λ_{max}^{EtOH}	266 mμ (4.42)*	
	289 (3.46)	253(4.75)
	300 (3.41)	295(3.80)
	384 (3.56)	358(3.40)
$\nu_{C=O}^{CHCl_3}$	1770, 1630 cm^{-1}	1770, 1685 cm^{-1}

* log ε enclosed in parenthesis

same arrangement of skeletal double bonds. The IR absorption of the annular carbonyl group in the diacetate **9** is observed at 1685 cm^{-1}, which is too high a wave-number for what would be expected from diacetates of the type **2a** or **2b**, and therefore the three compounds should be represented by the naphthalenoid structure **2** and not by **2a** or **2b**. In view of the close spectroscopic similarity between the model **2** and CHR, and their corresponding derivatives (compare Figs. 1–3 and **8**, **9**), it is permissible to infer that CHR and derivatives also have naphthalenoid skeletons.

Methyl ethers, isopropylidene derivatives and other simple CHR *derivatives*

When CHR is reacted with ethereal diazomethane, the 9-OH is methylated rather than the 8-OH to give the 6,9-dimethyl ether **10**, which further gives the 2,8,3′,4′-tetraacetate **11**. The ether **10** lacks the 15 ppm NMR signal characteristic of the chelated 9-OH, and the IR band due to C_1-carbonyl is seen at 1670 cm^{-1} (vs. 1635 cm^{-1} in CHR, KBr disk). The preferential methylation of the more strongly hydrogen-bonded 9-OH, which is rather unexpected, can be rationalized by assuming that attack is by the cation $CH_3N_2^+$ formed in the preliminary equilibrium[8] (Eq. 1).

$$A—H + CH_2N_2 \rightleftarrows A^- + CH_3N_2^+ \qquad \text{(Eq. 1)}$$

The existence of this preliminary equilibrium has been experimentally verified[9] by methylating deuterated 4-hydroxypyrimidine with diazomethane and observing the production of 3-N-methyl-4-oxopyrimidine in which the methyl group is deuterated to various extents, i.e., $—CH_3$, $—CH_2D$, $—CHD_2$, $—CD_3$ (checked by mass spectrometry). In the present case, the diazonium cation formed in Eq. 1 would be in the vicinity of high nucleophilicity in the transient CHR dianion, namely, near C-6 and C-9 for the reason of charge distribution, and then the reaction will proceed via an S_N2 type route.[9]

By treatment with anhydrous acetone and a trace of *p*-toluenesulfonic acid, CHR yielded the 3′,4′-isopropylidene derivative **12**; this isopropylidene derivative gave the 2,6,8-triacetate **13** and the 2,6,8,9-tetraacetate **14** upon acetylation with pyridine and acetic anhydride. The UV spectrum of the isopropylidene triacetate **13**

[8] F. Arndt, B. Eistert, R. Gompper and W. Walter, *Chem. Ber.* **94**, 2125 (1961); R. Gompper, in *Advances in Heterocyclic Chemistry* (Edited by A. R. Katrizky) p. 245. Academic Press (1963).

[9] Y. Inoue, N. Furutachi and K. Nakanishi, in preparation for *J. Org. Chem.*

was similar to that of the 2,6,8,3′,4′-pentaacetate **6**, while that of the isopropylidene tetraacetate **14** was similar to that of CHR-2,6,8,9,3′,4′-hexaacetate **7**, and this established the positions of the acetyl groups.

Dihydro-CHR (**15**) (Chart 1)

Reduction of CHR with sodium borohydride in methanol afforded dihydro-CHR (**15**), lacking the IR absorption of the saturated carbonyl group but having a UV spectrum superimposable on that of CHR. The minor product **15a** resulting from the borohydride reduction is presumably the epimer of **15** at C-2′ (see Experimental); this minor product was also obtained upon sodium borohydride reduction of 3′,4′-isopropylidene CHR **12** followed by acid treatment.

1-*Deoxo*-CHR (**18**) (Chart 1)

Upon catalytic hydrogenation of CHR with platinum oxide, a product with a typical naphthalenoid UV spectrum was obtained. However, in the solid state, the IR spectrum in the double bond stretching region consisted of bands at 1653, 1620 and 1600 cm^{-1}, and therefore this product **18** should be formulated as indicated in Chart 1, i.e., the C_9–OH adopts the oxo form and the C_2–OH and C_2′-carbonyl form a hemiketal. However, the hemiketal is cleaved and the nucleus reverts to the naphthalenoid type in its hexaacetate **19** and 3′,4′-isopropylidene tetraacetate **20**, as indicated by the UV spectra and IR band at 1735 cm^{-1} (C_2′-carbonyl).

Chromomyciquinone (**21**) (Chart 1)

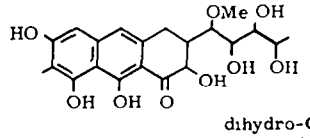
The naphthoquinone derivative, chromomyciquinone (CHQ) which was of vital importance in the structure elucidation of CHR, was first produced in poor yield from the sodium borohydride reduction of the noncrystalline CHR.* Later it was found that the yield could be greatly increased when the reaction mixture was exposed to air, and that its formation actually proceeded via 1-deoxo-CHR (**18**). Since the derivation of the structures of CHQ and its derivatives, and especially the part played by their NMR spectra, has already been discussed in a previous communication,[3] only the spectroscopic comparisons with model naphthoquinones that enabled one to establish the positions of the C_6–OH and C_7–Me groups will be discussed in the following.

The final choice between two alternative structures, **21** or **26**, was based on comparisons of UV and IR spectra with synthetic models, 2,5-dihydroxynaphthoquinone (**27**)[10–12] and 3,5-dihydroxynaphthoquinone (**28**).[12,13] The UV spectra of the two quinones are very similar in neutral solution,[14] but in 0·1N NaOH they can be readily differentiated and as shown in Fig. 4, the spectrum of CHQ is more similar to that of the 2,5-dihydroxy compound **27**. The same conclusion is deduced

* Structural studies of the chromophore were initially undertaken on CHQ rather than CHR because the latter could not be isolated crystalline.

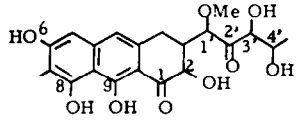
[10] F. Mylius, *Chem. Ber.* **18**, 463 (1885).
[11] R. H. Thomson, *J. Org. Chem.* **16**, 1082 (1951).
[12] J. W. Macleod and R. H. Thomson, *J. Org. Chem.* **25**, 36 (1960).
[13] L. F. Fieser and J. T. Dumn, *J. Amer. Chem. Soc.* **59**, 1016 (1937).
[14] M. Asano and J. Hase, *J. Pharm. Soc. Japan* **63**, 83 (1943).

CHART I



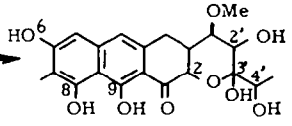
dihydro-CHR 15
2, 6, 8, 2', 3', 4'-hexa-OAc 16
2, 6, 8, 9, 2', 3', 4'-hepta-OAc 17

1.



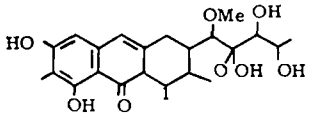
Chromomycinone 1 (CHR)

2.



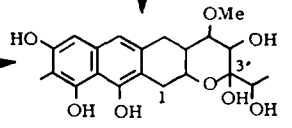
iso-CHR 29
6, 8, 9, 2', 4'-penta-OAc 30
3', 4'-isoPr * 31
3', 4'-isoPr-6, 8, 2'-tri-OAc 32
3', 4'-isoPr-6, 8, 9, 2'-tetra-OAc 33

3.



1-deoxo-CHR 18
2, 6, 8, 9, 3', 4'-hexa-OAc 19
3', 4'-isoPr-2, 6, 8, 9-tetra-OAc 20

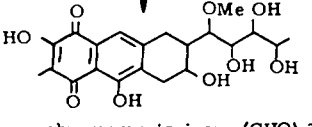
2.



1-deoxo-iso-CHR 34
3', 4'-isoPr-6, 8, 9, 2'-tetra-OAc 35

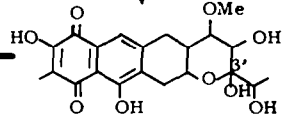
5.

4.



chromomycinone (CHQ) 21
2, 6, 9, 2', 3', 4'-hexa-OAc 22
leucoocta-OAc 23
3', 4'-isoPr 24
3', 4'-isoPr-2, 6, 9, 2'-tetra-OAc 25

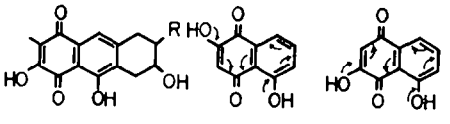
1.



3'-dehydro-CHQ 36
6, 9, 2', 4'-tetra-OAc 37
3', 4'-isoPr-6, 9, 2'-tri-OAc 38
3'-Me ketal 39
3'-Me ketal-6, 9, 2', 4'-tetra-OAc 40

REAGENTS
1. SBH, 2. K_2CO_3, 3. H_2/Pt, 4. SBH, air oxid., 5. K_2CO_3, air oxid.,

* isoPr: isopropylidene.



26 27 28

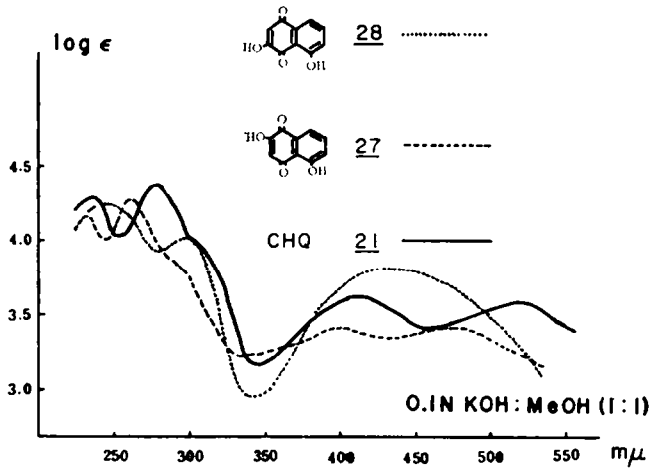


FIG. 4. UV spectra of 3,5-dihydroxynaphthoquinone (28), 2,5-dihydroxynaphthoquinone (27) and chromomyciquinone (21) in 0·1N KOH–MeOH (1:1).

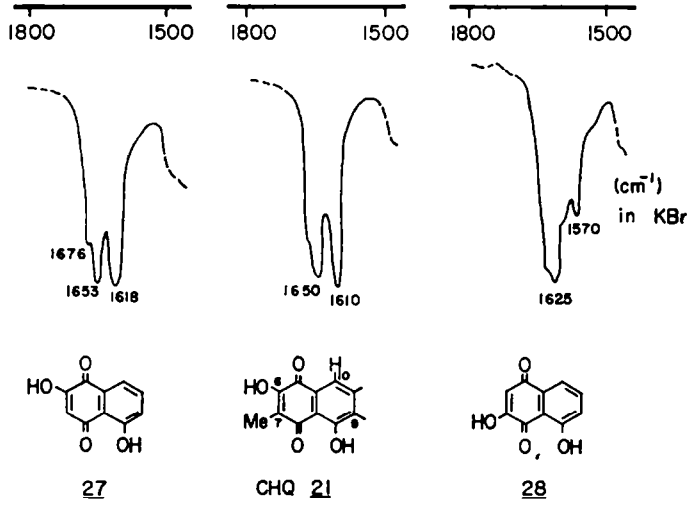


FIG. 5. IR spectra of 3,5-dihydroxynaphthoquinone (28), 2,5-dihydroxynaphthoquinone (27) and chromomyciquinone (21) in KBr.

from a comparison of IR spectra in the double bond stretching region (Fig. 5). Namely, the spectra of CHQ (21) and the model 27 have two strong bands whereas that of model 28 has only one broad absorption. Since the carbonyl stretching vibration would be making the major contribution to the mentioned absorptions, the difference may be rationalized, although in a very qualitative manner, by the arrows shown in formulas 27 and 28; in 27 the two hydroxyls are both conjugated to the same carbonyl group, whereas in 28 each hydroxyl is conjugated to different carbonyl groups so that the two absorb at more or less the same frequencies.

Isochromomycinone (29) (Chart 1)

Treatment of CHR (1) with aqueous potassium carbonate at room temperature resulted in isomerization to yield iso-CHR (29), which had a UV spectrum very

similar to that of CHR but lacked the 1720 cm^{-1} IR band of the saturated carbonyl group. Chemical and spectroscopic data of iso-CHR and its derivatives establish the structure of this isomer as **29**, the isomerization of the C-2′ and C-3′ functions presumably being caused by enolization and subsequent ketonization.

Acetylation furnished the pentaacetate **30**, which still showed an hydroxyl band in its IR; the NMR signals at 4·97 (quartet, J 6·5) and 5·15 ppm (doublet, J 9·5) could only be ascribed to the C-4′ and C-2′ protons in the expression **29**. Upon treatment with acetone and a trace of sulfuric acid, the isopropylidene derivative **31** was formed, which on acetylation furnished the triacetate **32** and tetraacetate **33**. The NMR spectrum of 3′,4′-isopropylidene-iso-CHR-6,8,2′-triacetate **32** (see Fig. 2 in Ref. 15) will be discussed in conjunction with the deduction of configurations at C-2, C-3 and C-1′;[15] however, it may be pointed out at this stage that the large coupling constants in iso-CHR derivatives, i.e., J_{23} *ca.* 12 c/s, $J_{31'}$ and $J_{1',2'}$, *ca.* 9 c/s, clearly show that the four protons attached to C-2, C-3, C-1′ and C-2′ are all axially oriented.

Support for the structure **29** is also obtained from chemical reactions. When iso-CHR was hydrogenated over platinum catalyst under conditions employed in the reduction of CHR (**1**) to 1-deoxo-CHR (**18**) (Chart 1), the oxygen function at C-1 was removed in a similar manner and 1-deoxoiso-CHR (**34**) was obtained. The same product **34** also resulted from alkali treatment of 1-deoxo-CHR (**18**). Furthermore, aerial oxidation of both 1-deoxo-CHR (**18**) and 1-deoxoiso-CHR (**34**) in aqueous 10% potassium carbonate for 48 hours afforded a naphthoquinone, having IR (3400, 1650, 1600 cm^{-1}) and UV (256, 300, 415 mμ) spectra closely resembling those of CHQ (**21**) and 2,5-dihydroxynaphthoquinone (**27**). The product can therefore be assigned the hemiketal structure **36** (no saturated IR carbonyl band) and named 3′-dehydro-CHQ.

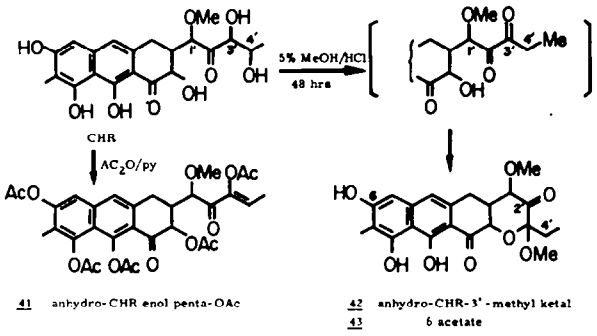
Treatment of **36** with methanolic hydrogen chloride gave in high yield the methyl ketal **39**, which was converted into its tetraacetate **40**; the same acetate was also obtained by ketalization of the tetraacetate **37**. These chemical conversions, as well as the NMR, IR and UV spectra of derivatives **27** to **40** (see Experimental) fully corroborate the structure shown. Finally, reduction of 3′-dehydro-CHQ (**36**) with sodium borohydride afforded CHQ.

The anhydrochromomycinone derivatives **41** *and* **42**

As already described, acetylation of CHR with pyridine and acetic anhydride afforded the hexaacetate **7**; however, this acetate was obtained when the reaction mixture was purified by chromatography on silica gel that had been pre-treated with 1% oxalic acid. On the other hand, passage of the mixture through a column of untreated silica gel gave in addition to the hexaacetate **7**, another product, which, although it could not be induced to crystallize, gave only a single spot on TLC. The IR spectrum had a band at 1700 cm^{-1} instead of 1720 cm^{-1} (in CHR), while the NMR spectrum exhibited signals at 1·80 ppm (3H, doublet, J 6·5 c/s) and 6·60 ppm (1H, quartet, J 6·5 c/s); the UV spectrum was very similar to that of the hexaacetate **7** excepting for the appearance of an additional shoulder around 242 mμ. The product is accordingly anhydro-CHR enol pentaacetate having structure **41**.

[15] M. Miyamoto, K. Morita, Y. Kawamatsu, K. Kawashima and K. Nakanishi, *Tetrahedron* **22**, in press (1966).

ANHYDRO CHROMOMYCINONES



41 anhydro-CHR enol penta-OAc

42 anhydro-CHR-3'-methyl ketal

43 6 acetate

It had been noticed for some time that hydrolysis of chromomycin A_3 with methanolic hydrogen chloride gave rise to a substance which seemed to originate from CHR, the major hydrolysis product. The nature of this substance was determined as follows. When CHR itself was treated with methanolic hydrogen chloride and the reaction followed by TLC, it was found that the starting material disappeared after 48 hours, and that a new substance with a greater mobility was produced. Column chromatography of the reaction mixture on silica gel (pretreated with 1% oxalic acid) afforded a crystalline product to which the anhydro ketal structure **42** has been assigned on the basis of the following spectroscopic properties: the UV spectrum was very similar to that of CHR; the IR spectrum lacked the 1720 cm^{-1} band present in CHR but instead showed an absorption at 1740 cm^{-1}, the NMR spectrum of its 6-monoacetate **43** (with low field signal at 9·94 and 15·30 ppm due to chelated hydroxyls) clearly indicated the presence of an ethyl group and one additional methoxyl group. The formation of anhydro-CHR-3'-methyl ketal **42** can best be accounted for by dehydration of CHR and subsequent cyclic ketalization.

2-*Deoxy*-CHR *pentaacetate* (**44**)

CHR tetraacetate **5** and CHR pentaacetate **6** afforded no clearcut product when treated with chromous acetate[16] probably because of their tendency to form chelates with the reagent. However, the hexaacetate **7** was smoothly reduced by this reagent and gave 2-deoxy-CHR 6,8,9,3',4'-pentaacetate (**44**). The chemical shifts of the five acetoxyl peaks in the NMR spectrum unambiguously showed that it was the 2-acetoxyl group that was eliminated and not the other α-keto acetoxyl group in the side chain (see Table 1).

Degradative products of CHR

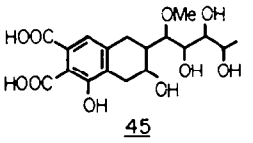
Zinc dust distillation of CHR gave anthracene and 2-methylanthracene, which were identified by comparison with authentic samples by VPC. The production of anthracenes was informative in that it suggested the gross structure of the chromophore during the initial stages of structural studies.

Careful oxidation of CHQ **21** with alkaline hydrogen peroxide cleaved the quinonoid ring to afford a phenolic dicarboxylic acid **45** which did not possess an aromatic methyl, as shown by its NMR spectrum; this evidence was useful since it located the aromatic methyl group in the quinonoid ring rather than in the center ring.

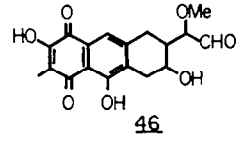
[16] W. Cole, P. B. Hirschman and J. W. Corecran, *J. Org. Chem.* **20**, 572 (1955).

When CHQ **21** was oxidized with sodium periodate, a mixture of the trisnor aldehyde **46** and the hemiacetal **47** was produced; the aldehyde **46** could be converted into its hemiacetal **47** either with aqueous sodium bicarbonate or with boiling ethanol–hydrochloric acid.

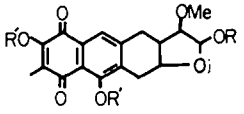
The hemiacetal **47** gave the methyl acetal **48** when boiled in methanolic hydrogen chloride. The methyl acetal **48** reverted to the starting hemiacetal **47** in boiling acetic acid. Finally, acetylation of the methyl acetal afforded the corresponding diacetate **49**.



45



46



47 R = R′ = H
48 R = Me, R′ = H
49 R = Me, R′ = Ac

Some comments on the NMR *spectra*

A striking feature noticed in the NMR spectra of the acetates of CHR and related compounds was that in spite of the number of methyl peaks appearing in the narrow range between 2·0 to 2·5 ppm, in every case they were clearly separated and easily characterized by their relative chemical shifts (see for example Fig. 6). As shown in Table 1, the chemical shift of each acetoxyl group varies little from compound to compound. It should be pointed out that determination of the point of attachment of each of these acetoxyl groups was based solely on UV spectra (Fig. 2), the IR carbonyl bands (Fig. 3) and the two low field NMR signals at *ca.* 10 and 16 ppm due to the chelated C-8 and C-9 hydroxyl groups (Fig. 7), and not on the chemical shifts of the acetoxyl groups. As might be expected, the C_9-acetoxyl had the lowest chemical shift (2·5 ppm) owing to the combined effects of the aromatic ring current and the peri-positioned carbonyl group; the next two peaks are those arising from the C_8-(2·4 ppm) and C_6-acetoxyls (2·35 ppm). This is followed by the two α-keto acetoxyls at C-2 (2·3 ppm) and C-3′ (2·2 ppm) and finally the C_4-acetoxyl (2·0 ppm). The C-7 aromatic methyl signal is at 2·1 ppm, i.e., between the 2·2 and 2·0 ppm peaks, and can be readily distinguished because of the low peak height due to long-range coupling to the C-5 aromatic proton (see Fig. 6). Once this orderly sequence was noticed, it could be employed with advantage in providing corroborative proof of the acetoxyl position in the CHR triacetate (Table 1), which resulted from hydrolysis of chromomycin A_3 hexaacetate and which played a key role in deducing the point of attachment of the sugar residues.[17] The same regularity is observed in the NMR spectrum of CHR-chromose D peracetate[17] (Table 1).

The chemical shifts *in italics* in the table have suffered small shifts due to a change in environment of the acetoxyl group. For example in the two 1-deoxo-CHR acetates **19** and **20**, the C-9 and C-2 acetoxyl groups are shifted to higher fields to the

[17] M. Miyamoto, Y. Kawamatsu, K. Kawashima, M. Shinohara and K. Nakanishi, *Tetrahedron Letters* 545 (1966); see also *Tetrahedron* **22**, in press (1966).

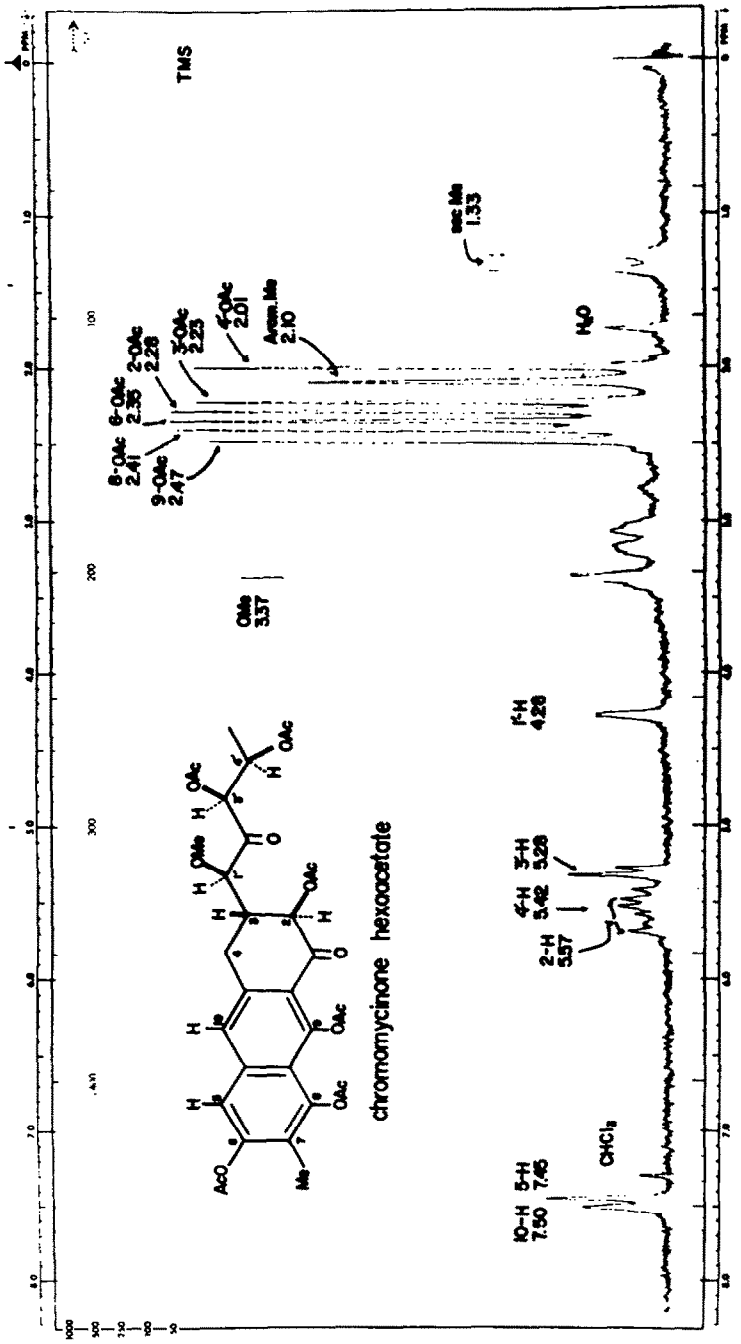
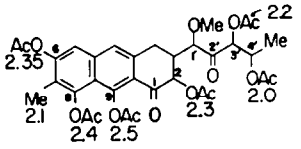


FIG. 6. NMR spectrum of chromomycinone hexaacetate in $CDCl_3$, ppm from TMS, 60 Mc.

TABLE 1. CHEMICAL SHIFTS OF ACETOXYL AND AROMATIC METHYL GROUPS IN CHR DERIVATIVES.

The numerals in the Fig. denote average chemical shifts of respective groups in ppm. The chemical shifts in italics in the Table indicate that these particular acetoxyl groups are in a different environment.



CHR acetates	9	8	6	2	3′	7Me[1]	4′
5 tetra-			2·35	2·32	2·23	2·13	2·02
6 penta-		2·38	2·35	2·32	2·23	2·08	2·02
7 hexa-	2·47	2·41	2·35	2·28	2·23	2·10	2·01
11 6,9-OMe-tetra-		2·38		2·31	2·24	2·10	2·02
13 3′,4′-isopropylidene-tri-		2·39	2·37	2·30		2·12	
14 3′,4′-isopropylidene-tetra-	2·48	2·40	2·36	2·27		2·11	
16 dihydro, hexa-[2]		2·36	2·33	2·27	*2·08*	2·05	2·03
17 dihydro, hepta-[3]	2·48	2·41	2·39	2·28	*2·11*	2·11	2·06
19 1-deoxo, hexa-	*2·39*	2·39	2·34	*2·12*	2·23	2·08	2·02
20 1-deoxo-isopropylidene-tetra	*2·36*	2·36	2·30	*2·07*		2·06	
41 anhydro, penta-	2·49	2·41	2·36	2·30	*2·30*[4]	2·09	
44 2-deoxy, penta-	2·47	2·42	2·34		2·20	2·10	2·00
tri-[5]		2·41			2·21	2·05	1·97
CHR-chromose-D peracetate[5,6]	2·48	2·39		2·28	2·23	2·12	2·03

[1] Always low peak height.
[2] 2′-OAc at 2·08 ppm.
[3] 2′-OAc at 2·11 ppm.
[4] Enol acetate.
[5] Cf. Ref. 17.
[6] Chromose D OAc at 2·17 and 1·99 ppm.

extent of roughly 0·1 and 0·2 ppm, respectively, because of the disappearance of the anisotropy due to the C-1 keto group.

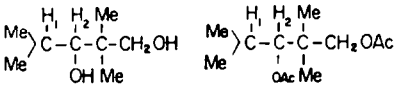
Another feature noticed was the unusually small coupling of the adjacent protons in the side-chain of CHR derivatives (Table 2). This is due to some extent to the presence of the electronegative C-2′ keto group because it has been reported, both on theoretical grounds[18] and experimental observations,[19] that electronegative groups decrease the coupling constants. Another factor is the dihedral angle between the two adjacent C—H bonds.[20] A substituted ethane, at ordinary temperature, generally exists as a mixture of rapidly interconverting rotational isomers, and the observed coupling constants will be the weighted mean value of the coupling constants of each distinct rotamer. Therefore, if the coupling constants for the individual isomers can be obtained, the population of each rotamer can be estimated. The coupling constants for the *trans* and *gauche* forms of ethane derivatives has been estimated to be 11–13 c/s

[18] M. Karplus, *J. Amer. Chem. Soc.* **85**, 2870 (1963).
[19] C. N. Banwell and N. Sheppard, *Discussions Faraday Soc.* No. 34, 115 (1962); T. Schaefer, *Canad. J. Chem.* **40**, 1 (1962); P. Laszlo and P. von Schleyer, *Bull. Soc. Chim. France* 87 (1964); K. L. Williamson, *J. Amer. Chem. Soc.* **85**, 516 (1963).
[20] M. Karplus, *J. Chem. Phys.* **30**, 11 (1959).

TABLE 2. J (IN c/s) BETWEEN ADJACENT PROTONS IN THE SIDE-CHAIN OF CHR DERIVATIVES.

Compound	$J_{1'}$	$J_{3'4'}$
CHR-acetates **5**, **6**, **7**	*ca.* 1	3·0
CHR-3',4'-isopropylidene-2,6,8,9-tetraacetate **14**	1·5	—
1-deoxo-CHR hexaacetate **19**	2	3·0
2-deoxy-CHR pentaacetate **44**	2	2·0

and 1–3 c/s, respectively,[21] while the usual value for a freely rotating HC—CH bond is 7–8 c/s. The small J values observed in the present case were first attributed to small dihedral angles between the C—H bonds in question; however, the side-chain seemed to be devoid of steric hindrance to free rotation, and there seemed to be



50 J_{12} = 2.6 cps **51** J_{12} = 3.4 cps

no particular reason that prevented the C-3/C-1' or C-3'/C-4' pair of protons to adopt an s-*trans* arrangement. Presence of the acetoxyl group at C-2 was considered as one factor giving rise to some steric restriction, but this can be ruled out since the same small J values are observed in 2-deoxy-CHR pentaacetate **44** (Table 2) which is not substituted at this position. Furthermore, a similar anomaly was observed in the acyclic diol **50**; hydrogen-bonding cannot be involved because the J_{12} is also small in its diacetate **51**.[22]

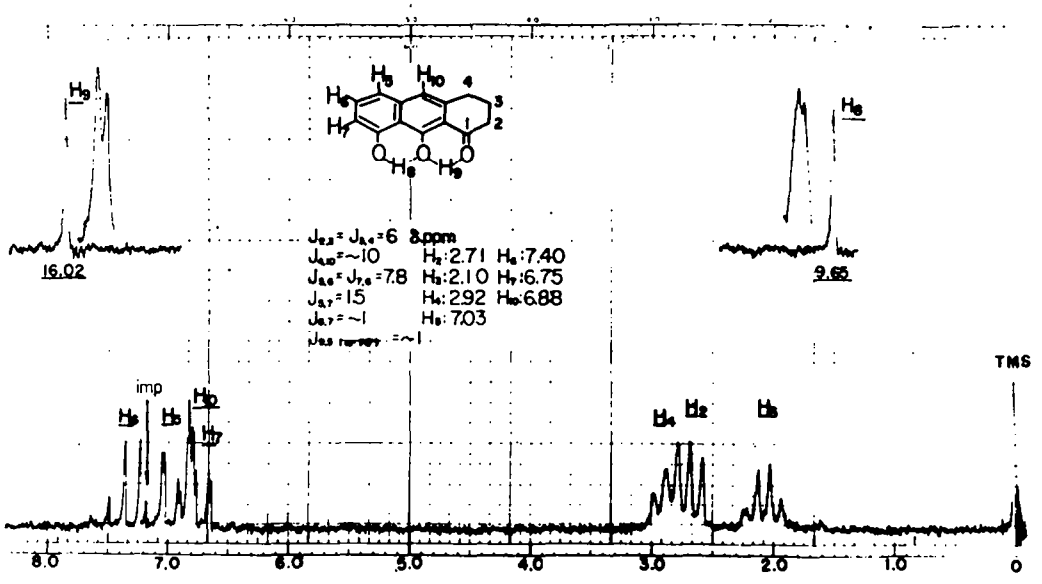


FIG. 7. NMR spectrum of 1-keto-8,9-dihydroxy-1,2,3,4-tetrahydroanthracene (**2**) in $CDCl_3$, ppm from TMS, 60 Mc. Part spectrum shows low field peak, original and expanded.

[21] A. A. Bothner-By and C. Naar-Colin, *J. Amer. Chem. Soc.* **84**, 743 (1962).
[22] Unpublished results, Tohoku University.

Finally, the NMR spectrum of the model compound, 1-keto-8,9-dihydroxy-1,2,3,4-tetrahydroanthracene **2**, is shown in Fig. 7; it can be analysed in a straightforward manner, the results also being tabulated in the Fig. It is of interest to note that there is a slight splitting in the two low field peaks at 9·65 and 16·02 ppm. The 9·65 ppm peak assigned to the C-8 hydroxyl is further coupled to the aromatic proton at C-6; similar coupling through five bonds have been frequently encountered.[23] However, the lower signal due to C_9–OH is also subject to long-range coupling, presumably to the C-5 proton, through six bonds.

EXPERIMENTAL

The IR spectra were taken on a Hitachi EPI-S2 instrument. UV spectra were recorded for EtOH solution on a Hitachi EPS-2. NMR spectra were taken on a Varian A-60 instrument and the chemical shifts are given in ppm relative to internal TMS; s, singlet; d, doublet; t, triplet; q, quartet; coupling constants are given in c/s.

Chromomycinone (**1**)

(a) Methanolic HCl (5%, 250 ml) was added to a solution of chromomycin A_3 (15 g) in MeOH (50 ml). The reaction mixture was allowed to stand for about 2 hr at room temp. The solution was poured into ice-water (1·5 l.), and extracted with ether three times. The ether extract was washed with saturated NaClaq and dried (Na_2SO_4). After removal of the solvent, the residue was washed with $CHCl_3$ and dissolved in MeOH (100 ml). After removal of insoluble material, the solution was treated with AcOH (100 ml) and concentrated under red. press. at 60°. During this procedure, yellow crystals precipitated in a flask, which were collected and dried overnight under red. press. at 50°, m.p. 175–178°. (Found: C, 55·44; H, 5·97. $C_{21}H_{24}O_9 \cdot 2CH_3COOH$ requires: C, 55·55; H, 5·95%.) λ_{max}^{EtOH} (log ε) 232 mμ (4·38), 282 (4·60), 326 (3·85), 340 (3·85), 412 (4·01). The AcOH was removed by heating at 100° under red. press. The IR spectrum of the acetic acid free specimen is shown in Fig. 8.

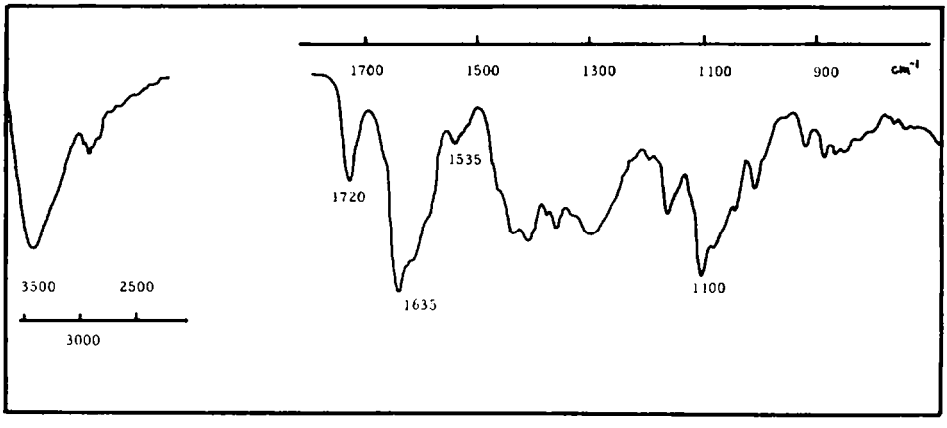


FIG. 8. IR spectrum of chromomycinone in KBr.

(b) Chromomycin A_3 was heated in 50% AcOH for 3 hr, the solution was concentrated, the residue was extracted with AcOEt, the extract was washed thoroughly with water and concentrated. The residue was dissolved in a small amount of AcOEt and chromatographed on silica gel containing 1% oxalic acid, the column being eluted with AcOEt–1% oxalic acid. The eluate corresponding to the yellow band was washed with water, dried, and concentrated to give chromomycinone. The yield was poor.

[23] S. Sternhell, *Rev. Pure and Appl. Chem.* **14**, 15 (1964).

1-Keto-8,9-dihydroxy-1,2,3,4-tetrahydroanthracene (2)

A solution of chrysanthrone—9-keto-1,8-dihydroxy-9,10-dihydroanthracene—(1 g) in AcOH (200 ml) was hydrogenated over Adams catalyst (300 mg) until 200 ml of H_2 had been absorbed (about 2 hr). The catalyst was filtered rapidly and the solvent was removed under red. press. to give a solid. Recrystallization from EtOH yielded needles (120 mg), m.p. 120°. (Found: C, 73·68; H, 5·22. $C_{14}H_{12}O_3$ requires: C, 73·67; H, 5·30%.) ν_{max}^{KBr} 3400, 1630, 1580 cm^{-1}. The UV and NMR spectra are shown in Figs. 1b and 7.

Chrysanthrone (4)

Compound 4 was prepared from 3 according to the procedure described by Schrobsdorfe.[5] A mixture of 3 (5 g), red P (15 g) and HI (150 g) was boiled for 1 hr. The HI was removed by filtration and the precipitates were extracted with acetone. The extract was dried up and the residue was recrystallized from $CHCl_3$ to give 3·5 g of 4, m.p. 179° (lit.[5] 176–177°), orange flakes. (Found: C, 74·06; H, 4·58. Calc. for $C_{14}H_{10}O_3$: C, 74·33; H, 4·45%.)

Chromomycinone acetates

(a) *Chromomycinone tetraacetate* 5. *p*-Toluenesulfonic acid (90 mg) was added to a suspension of chromomycinone (300 mg) in acetic anhydride (15 ml). The yellow-orange solution was left for 60 min at 80° and then poured into ice. The precipitates were collected, washed with water and dried over P_2O_5 (330 mg). The precipitate showed a strong yellow spot with a tail of green fluorescence on a thin layer chromatoplate of silica gel treated with 1% oxalic acid and developed with $CHCl_3$: AcOEt = 10:3. Precipitates were dissolved in $CHCl_3$ and this was chromatographed on silica gel treated with 1% oxalic acid, and eluted with $CHCl_3$–AcOEt (10:2). Fractions exhibiting a single spot on a thin layer plate were collected and washed with water to remove the oxalic acid. After treatment with anhydrous Na_2SO_4 the solution was evaporated to dryness. Recrystallization of the residue from EtOH afforded crystals, 60 mg, m.p. 213–214°. (Found: C, 59·20; H, 5·48. $C_{29}H_{32}O_{13}$ requires: C, 59·18; H, 5·48%.) λ_{max}^{EtOH} (log ε) 273 mμ (4·71), 420 (3·99). $\nu_{max}^{CHCl_3}$ 3400, 1740, 1632, 1577, 1514 cm^{-1}. NMR ($CDCl_3$) δ 1·34 (3H, d, J 6, sec Me), 2·02 (3H, s, OAc, 2·13 (3H, s, arom Me), 2·23 (3H, s, OAc), 2·32 (3H, s, OAc), 2·35 (3H, s, OAc), 3·40 (3H, s, OMe), 4·21 (1H, d, J 1·5, $H_{1'}$), 5·29 (1H, d, J 3, $H_{3'}$), 5·48 (1H, q, $J_{3'4'}$ = 3, $J_{4'5'}$ = 6, $H_{4'}$), 5·67 (1H, d, J 11·5, H_3), 6·84 (2H, s, arom H), 9·72 (1H, s, C_8–OH), 15·20 (1H, s, C_9–OH).

(b) *Chromomycinone pentaacetate* 6. *p*-Toluenesulfonic acid (50 mg) was added to a suspension of 1 (500 mg) in acetic anhydride (50 ml), the solution was kept at 80° on a water bath for 10 hr, poured into ice-water, and extracted with ether. The ether extract was washed with water, dried (Na_2SO_4) and concentrated to dryness under red. press.; the residue revealed a main spot having a strong green fluorescence along with several minor spots on a thin layer chromatoplate (silica gel treated with 1% oxalic acid, and developed with $CHCl_3$–acetone–EtOH = 100:3:0·1). The $CHCl_3$ solution of the residue was chromatographed on silica gel pre-treated with 1% oxalic acid, and eluted with the solvent system mentioned above. Fractions showing one spot on TLC were collected, washed with water, dried and evaporated under red. press. to give an amorphous solid (200 mg). Recrystallization from MeOH gave a small amount of crystals, m.p. 154–155°. (Found: C, 58·87; H, 5·70. $C_{31}H_{34}O_{14}$ requires: C, 58·88; H, 5·42%.) λ_{max}^{EtOH} (log ε) 263 mμ (4·59), 272 (4·60), 390 (4·07). $\nu_{max}^{CHCl_3}$ 3350, 1750, 1630, 1570 cm^{-1}. NMR ($CDCl_3$) δ 1·34 (3H, d, J 6·5), 2·02 (3H, s), 2·08 (3H, s), 2·23 (3H, s), 2·32 (3H, s), 2·35 (3H, s), 2·38 (3H, s), 3·39 (3H, s), 4·20 (1H, d, J 1·0), 5·29 (1H, d, J 3·0), 6·90 (1H, s), 7·27 (1H, s), 14·10 (1H, s).

(c) *Chromomycinone hexaacetate* 7. Compound 1 (300 mg) was dissolved in pyridine (5 ml) and acetic anhydride (5 ml) and set aside overnight at room temp. The reaction mixture was poured into ice-water, and extracted with ether. The ether solution was washed, dried and evaporated to dryness under red. press. The $CHCl_3$ solution of the resulting residue was purified by chromatography on silica gel treated with 1% oxalic acid to afford an amorphous solid (200 mg) which showed a single spot on TLC. Recrystallization from MeOH gave crystals, m.p. 184°. (Found: C, 59·13; H, 5·39. $C_{33}H_{36}O_{15}$ requires: C, 58·91; H, 5·39%.) λ_{max}^{EtOH} (log ε) 260 mμ (4·80), 302 (3·87), 364 (3·46). $\nu_{max}^{CHCl_3}$ 1750, 1690, 1630, 1608 cm^{-1}. NMR ($CDCl_3$) δ 1·33 (3H, d, J 6·5), 2·01 (3H, s, OAc), 2·10 (3H, s, arom Me), 2·23 (3H, s, OAc), 2·28 (3H, s, OAc), 2·35 (3H, s, OAc), 2·41 (3H, s, OAc), 2·47 (3H, s, OAc), 3·37 (3H, s, OMe), 4·28 (1H, d, J 1·5), 5·28 (1H, d, J 3), 5·42 (1H, m), 5·57 (1H, d, J 9·5), 7·45 (1H, s, arom H), 7·50 (1H, s, arom H).

Acetylation of the tetrahydroanthracene **2**

(a) *The 8-acetate.* Compound **2** (100 mg) was refluxed for 15 min in acetic anhydride containing a small amount of unfused AcONa, and the reaction mixture was poured into water. The precipitates were collected and recrystallized from EtOH to give 90 mg of pale yellow crystals, m.p. 139.° (Found: C, 70·94; H, 5·20. $C_{16}H_{14}O_4$ requires: C, 71·10; H, 5·22%.) λ_{max}^{EtOH} (log ε) 266 mμ (4·42), 289 (3·46), 300 (3·41), 384 (3·56). ν_{max}^{KBr} 3450, 1770, 1635 (sh), 1630, 1580, 1200, 1040, 885 cm^{-1}.

(b) *The 8,9-diacetate.* Compound **2** (100 mg) was acetylated with pyridine and acetic anhydride; recrystallization of the product from EtOH gave 95 mg of pale yellow crystals, m.p. 191°. (Found: C, 69·32; H, 5·19. $C_{18}H_{16}O_5$ requires: C, 69·22; H, 5·16%.) λ_{max}^{EtOH} (log ε) 253 mμ (4·75), 286 (sh), 295 (3·80), 306 (sh), 358 (3·40). ν_{max}^{KBr} 1770, 1685, 1630, 1600, 1210, 1045, 895 cm^{-1}.

Chromomycinone dimethyl ether **10**

Ethereal diazomethane (2 ml) was added to a suspension of **1** (200 mg) in EtOH to give a clear solution. This was further treated with 1 ml of diazomethane, set aside at room temp for 1 hr, and was evaporated to an oil which showed two main spots on TLC (silica gel treated with 1% oxalic acid; developed with AcOEt–$CHCl_3$ 10:3). Ethereal diazomethane (1 ml) was added to the oil. As the ether evaporated, crystals started to appear. The crystals were recrystallized from n-hexane–acetone, 100 mg, m.p. 146–148° (dec.). (Found: C, 61·35; H, 6·40. $C_{32}H_{28}O_9$ requires: C, 61·60; H, 6·29%.) ν_{max}^{KBr} 1720, 1670, 1630, 1605, 1564, 1505, 1108 cm^{-1}. NMR ($CDCl_3$) δ 1·37 (3H, d, J 7), 2·17 (3H, s, arom Me), 3·57 (3H, s, OMe), 3·88 (3H, s, OMe), 4·00 (3H, s, OMe), 4·80 (1H, d, J 2·5), 6·50 (1H, s, arom H), 7·16 (1H, s, arom H).

Chromomycinone 6,9-dimethyl ether tetraacetate **11**

The above-mentioned dimethyl ether **10** was acetylated with pyridine and acetic anhydride according to conventional methods, and a $CHCl_3$ solution of the acetate was then chromatographed on silica gel containing 1% oxalic acid and eluted with $CHCl_3$. The main fraction was washed with water, dried, and evaporated to dryness to give the tetraacetate **11**; because of the minute amount only the NMR spectrum was measured. NMR ($CDCl_3$) δ 1·35 (3H, d, J 7 Me), 2·02 (3H, s, OAc), 2·10 (3H, s, arom Me), 2·24 (3H, s, OAc), 2·31 (3H, s, OAc), 2·38 (3H, s, OAc), 3·33 (3H, s, OMe), 3·72 (3H, s, OMe), 3·85 (3H, s, OMe), 6·63 (1H, s, arom H), 7·02 (1H, s, arom H).

Isopropylidenechromomycinone (**12**)

Compound **1** (300 mg) was dissolved in acetone (20 ml) containing a small amount of *p*-toluenesulfonic acid. The reaction mixture was set aside at room temp for 15 min. Water was added to the solution and extracted with ether. The ether extract was washed with water, dried and evaporated to dryness. The residue was chromatographed on a column packed with cellulose powder (300 mesh, 100 g) and eluted with $CHCl_3$–acetone–EtOH (100:3:0·1). Evaporation of the solvent afforded solids (250 mg). Recrystallization from MeOH gave crystals, m.p. 118–120° (dec.). (Found: C, 60·48; H, 6·39. $C_{24}H_{28}O_9 \cdot H_2O$ requires: C, 60·24; H, 6·32%.) λ_{max}^{EtOH} (log ε) 232 mμ (4·37), 280 (4·59), 322 (3·79), 410 (3·97). ν_{max}^{KBr} 3450, 1635, 1587 cm^{-1}. NMR ($CDCl_3$) δ 1·42 (9H, s, Me), 2·19 (3H, s), 3·51 (3H, s, OMe), 6·42 (1H, s, arom H), 6·53 (1H, s, arom H).

Isopropylidenechromomycinone acetates **13** *and* **14**

Compound **12** (400 mg) was dissolved in a mixture of pyridine (3 ml) and acetic anhydride (3 ml), and was allowed to stand at room temp for 3 hr. Excess of acetic anhydride was decomposed with MeOH. The reaction mixture was treated with water, extracted with ether, and the extract was washed with water and evaporated to dryness (450 mg). The residue was chromatographed on silica gel (200 g) and eluted with $CHCl_3$–acetone–EtOH (100:3:0·1) when two fractions were obtained. Each fraction gave one spot on TLC.

(a) *Isopropylidenechromomycinone triacetate* **13**. After removal of the solvent, the less polar fraction gave a yellow residue (94 mg), which was found to be a triacetate from its NMR spectrum. (Found: C, 61·12; H, 5·76. $C_{30}H_{34}O_{12}$ requires: C, 61·44; H, 5·84%.) λ_{max}^{EtOH} (log ε) 264 mμ (4·59), 272 (4·62), 293 (3·83), 304 (3·90), 390 (3·77). $\nu_{max}^{CHCl_3}$ 3500, 1745, 1631, 1567 cm^{-1}. NMR ($CDCl_3$) δ 1·32 (9H, broad s, Me), 2·12 (3H, s, arom Me), 2·30, 2·37, 2·39 (all 3H, s, OAc), 3·42 (3H, s, OMe).

(b) *Isopropylidenechromomycinone tetraacetate* **14**. The second fraction from the column was evaporated to an amorphous residue (230 mg), which was characterized as the tetraacetate from the NMR data. (Found: C, 61·03; H, 5·80. $C_{38}H_{36}O_{13}$ requires: C, 61·14; H, 5·73%.) λ_{max}^{EtOH} (log ε) 260 mμ (4·84), 301 (3·80), 360 (3·47). $\nu_{max}^{CHCl_3}$ 1770, 1710, 1645, 1610 cm^{-1}. NMR ($CDCl_3$) δ 1·43 (9H), 2·11 (3H, s), 2·27 (3H, s), 2·36 (3H, s), 2·40 (3H, s), 2·48 (3H, s), 3·39 (3H, s), 4·39 (1H, d, J 1·5), 5·58 (1H, d, J 12), 7·44 (1H, s), 7·50 (1H, s).

Dihydrochromomycinone (**15**)—$NaBH_4$ *reduction of* **1**

To a solution of **1** (1·8 g) in MeOH (45 ml) was added $NaBH_4$ in small portions with stirring and cooling in ice-water. The addition of the hydride was continued until **1** could not be detected on TLC. At this stage, dil. HCl was added to decompose the excess hydride. The reaction mixture was poured into water, extracted with AcOEt, and the extract was washed with water, dried and evaporated to dryness. The resulting solid was washed with ether and dried, 1·3 g. Crystallization from MeOH afforded two kinds of crystals which were separated by fractional crystallization. The major component, dihydrochromomycinone (**15**) (orange plates, more soluble) melted at 216–218° (dec.). (Found: C, 57·53; H, 6·16. $C_{31}H_{36}O_9 \cdot H_2O$ requires: C, 57·26; H, 6·41%.) λ_{max}^{EtOH} (log ε) 231 mμ (4·37), 280 (4·57), 325 (3·81), 340 (3·80), 410 (3·96). ν_{max}^{KBr} 3350, 1614, 1591 cm^{-1}. The minor component **15a** (less soluble) seems to be the $C_{9'}$-epimer, yellow fine needles, m.p. 225–228° (dec.). (Found: C, 59·57; H, 6·17. $C_{31}H_{36}O_9$ requires: C, 59·71; H, 6·20%.) λ_{max}^{EtOH} (log ε) 231 mμ (4·36), 281 (4·58), 326 (3·82), 340 (3·83), 413 (3·98). ν_{max}^{KBr} 3350, 1642, 1599, 1582 (sh) cm^{-1}.

The epimer **15a** was also obtained by another method. Compound **12** (2·0 g) was treated similarly with $NaBH_4$ to yield a reduction product (1·3 g), which was dissolved in 70% AcOH (30 ml) and heated at 60° for 1·5 hr. Evaporation of the solvent followed by crystallization from MeOH afforded needles (1·0 g), which turned out to be identical in all respects with **15a** described above.

Dihydrochromomycinone acetates

(a) *Dihydrochromomycinone hexaacetate* **16**. *p*-Toluenesulfonic acid (200 mg) was added to a suspension of **15** (560 mg) in acetic anhydride (12 ml). The reaction mixture was heated on a water bath for 1·5 hr. After cooling, it was poured into ice-water and extracted with ether. The ether extract was washed with water, dried and evaporated to dryness under red. press. Purification of the residue by passage through a column packed with silica gel treated with 1% oxalic acid, afforded an amorphous material, which showed a single spot on TLC. (Found: C, 58·41; H, 5·53. $C_{43}H_{48}O_{15}$ requires: C, 58·75; H, 5·68%.) λ_{max}^{EtOH} (log ε) 225 mμ (4·46), 272 (4·65), 304 (3·93), 392 (3·79). $\nu_{max}^{CHCl_3}$ 3400, 1764, 1733, 1631, 1572 cm^{-1}. NMR ($CDCl_3$) δ 1·26 (3H, d, J 7), 2·03 (3H, s, OAc), 2·05 (3H, s), 2·08 (6H, s), 2·27 (3H, s), 2·33, 2·36 (both 3H, s), 3·37 (3H, s, OMe).

(b) *Dihydrochromomycinone heptaacetate* **17**. Compound **15** (340 mg) was dissolved in a mixture of pyridine (5 ml) and acetic anhydride (5 ml), and was heated on a water bath for 45 min. The reaction mixture was poured into ice-water, and extracted with ether. The ether layer was washed with water, dried and concentrated to dryness. Purification of the residue by means of chromatography as described in (a) yielded 80 mg of the heptaacetate. (Found: C, 58·30; H, 5·61. $C_{45}H_{46}O_{16}$ requires: C, 58·65; H, 5·62%.) λ_{max}^{EtOH} (log ε) 260 mμ (4·82), 301 (3·89), 360 (3·45). $\nu_{max}^{CHCl_3}$ 1745, 1230, 1070 cm^{-1}. NMR ($CDCl_3$) δ 1·21 (3H, d, J 6·5), 2·06 (3H, s), 2·11 (9H, s), 2·28 (3H, s), 2·39 (3H, s), 2·41 (3H, s), 2·48 (3H, s), 3·40 (3H, s), 5·4 (4H), 7·49 (1H, s), 7·63 (1H, s).

1-*Deoxochromomycinone* (**18**)

A solution of **1** (1·5 g) in EtOH was hydrogenated over Adams catalyst until 2 moles of H_2 were uptaken. The catalyst was filtered and the solvent was removed to yield a solid. Recrystallization from EtOH afforded pale yellow flakes, m.p. 182° (dec.). (Found: C, 60·34; H, 6·49; OMe, 7·79. $C_{31}H_{36}O_8 \cdot \frac{1}{2}H_2O$ requires: C, 60·43; H, 6·47; OMe, 7·43%.) λ_{max}^{EtOH} (log ε) 244 mμ (4·36), 261 (3·87), 298 (3·78), 340 (3·82). ν_{max}^{KBr} 1653, 1620, 1600 cm^{-1}.

1-*Deoxochromomycinone hexaacetate* **19**

Compound **18** (70 mg) was treated with acetic anhydride (0·5 ml) and pyridine (1 ml) at room temp for 2 days. The reaction mixture was poured into ice-water. The precipitates were collected and recrystallized from EtOH to yield needles, m.p. 160°. (Found: C, 60·16; H, 5·74; OMe,

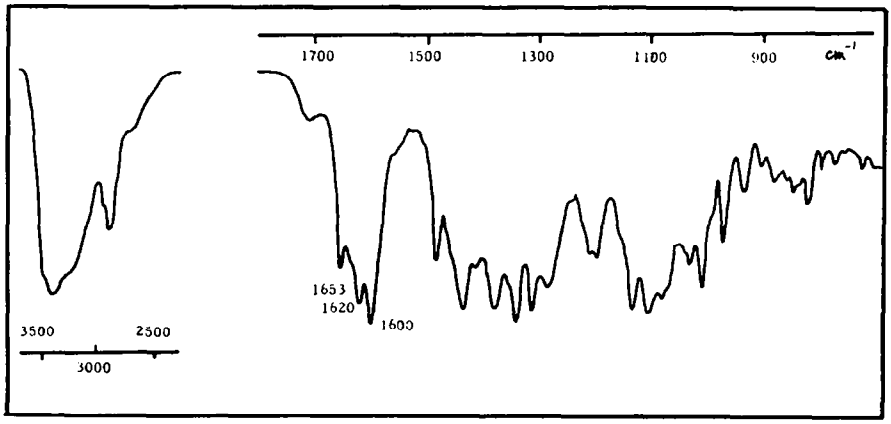


FIG. 9. IR spectrum of 1-deoxo-CHR in KBr.

4·83; OAc, 38·91. $C_{32}H_{38}O_{14}$ requires: C, 60·18; H, 5·77; OMe, 4·71; OAc, 39·20%.) λ_{max}^{EtOH} (log ε) 234 mμ (5·11), 275 (3·77), 283 (3·79), 290 (3·78). ν_{max}^{KBr} 1750, 1735, 1635, 1560 cm^{-1}. NMR ($CDCl_3$) δ 1·30 (3H, d, J 6·5), 2·02 (3H, s), 2·08 (3H, s), 2·12 (3H, s), 2·23 (3H, s), 2·34 (3H, s), 2·39 (6H, s), 3·31 (3H, s), 4·25 (1H, d, J 2), 5·35 (3H, m), 7·40 (1H, s), 7·45 (1H, s).

Isopropylidene-1-deoxochromomycinone-tetraacetate **20**

See Ref. 15 for preparation of this compound.

Chromomyciquinone (**21**)

(a) *From* **1**. $NaBH_4$ (10 g) was added in small portions to a solution of **1** (10 g) in EtOH (100 ml). After generation of H_2 had weakened, the reaction mixture was refluxed for 2 hr, transferred to a Petri dish and was exposed to air at room temp for 3 days. During this time, some water was added to the reaction mixture occasionally. Then it was poured into water, acidified with HCl and extracted with AcOEt. The extract was washed, dried and evaporated to yield an orange solid. Recrystallization from pyridine afforded orange needles (3·5 g), m.p. 209–210° (dec.), which were dried under red. press. at 100° for elemental analysis. (Found: C, 59·72; H, 6·16; OMe, 7·14. $C_{21}H_{26}O_9$ requires: C, 59·71; H, 6·20; OMe, 7·33%.) λ_{max}^{EtOH} (log ε) 256 mμ (4·30), 305 (3·10), 415 (3·68). IR, see Fig. 10. NMR (pyridine) δ 1·55 (3H, d, J 7), 2·21 (3H, s, arom Me), 3·76 (3H, s, OMe).

(b) *From* **18**. $NaBH_4$ (50 mg) was added to a solution of **18** (100 mg) in EtOH (3 ml), and the mixture was refluxed for 30 min. Working up as described above gave an orange solid (70 mg), which was identified as chromomyciquinone by IR spectra and mixture m.p. determination.

(c) *From 3'-dehydrochromomyciquinone* (**36**). A suspension of 250 mg **36** in 6 ml EtOH was treated with 1 g $NaBH_4$, and the mixture was boiled under N_2 for 4 hr, with occasional addition of EtOH. It was then poured onto a Petri dish, left at room temp for 10 hr and worked up as described in (a), to give 100 mg of chromomyciquinone.

Chromomyciquinone hexaacetate **22**

Compound **21** (150 mg) was dissolved in a mixture of pyridine (2 ml) and acetic anhydride (1 ml). The reaction mixture was set aside at room temp for 2 days, and poured into ice-water. Recrystallization of the precipitate from EtOH yielded yellow needles (110 mg), m.p. 183–185°. (Found: C, 58·79; H, 5·64; OMe, 5·02; OAc, 37·96. $C_{33}H_{38}O_{15}$ requires: C, 58·75; H, 5·64; OMe, 4·64; OAc, 38·28%.) λ_{max}^{EtOH} (log ε) 253 mμ (4·37), 275 (4·09), 355 (3·50). $\nu_{max}^{CHCl_3}$ 1770, 1740, 1670, 1660, 1600 cm^{-1}. NMR ($CDCl_3$) δ 1·12 (3H, d, J 6·5), 2·02 (3H, s), 2·08 (3H, s), 2·14 (9H, s), 2·40 (3H, s), 2·48 (3H, s), 3·00 (5H), 3·35 (3H, s), 5·2 (4H), 7·87 (1H, s).

Treatment of compd **21** (20 mg) with acetic anhydride (0·3 ml) in the presence of one drop of H_2SO_4 yielded the same acetate (20 mg).

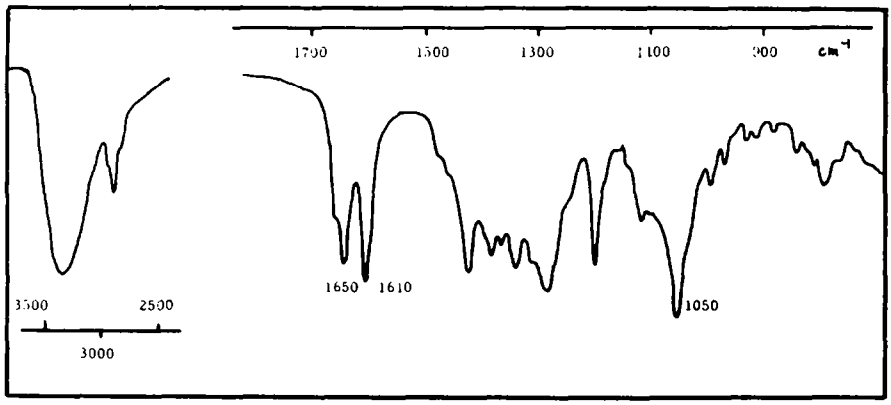


FIG. 10. IR spectrum of chromomyciquinone in KBr.

Chromomyciquinone leucooctaacetate **23**

Compound **22** (20 mg) was treated with acetic anhydride (1 ml), Zn dust (100 mg) and a small amount of AcONa. The reaction mixture was refluxed for 10 min, and after cooling was poured into ice-water. The precipitates were collected and purified on a column packed with silica gel to yield a white solid, 15 mg, m.p. 130°; it sublimed under red. press. above 200°. (Found: C, 58·34; H, 5·89; OMe, 4·22. $C_{37}H_{44}O_{17}$ requires: C, 58·42; H, 5·79; OMe, 4·08%.) λ_{max}^{EtOH} (log ε) 235 mμ (4·89), 285 (3·64). $\nu_{max}^{CCl_4}$ 1774, 1740, 1640, 1620 cm^{-1}. NMR ($CDCl_3$) δ phenolic acetoxyls at 2·36 (3H, s), 2·42 (6H, s), 2·48 (3H, s).

Isopropylidenechromomyciquinone **(24)**

A suspension of **21** (100 mg) in acetone (1 ml) was treated with conc. H_2SO_4. The reaction mixture was allowed to stand overnight at room temp. Then, water was poured into the reaction mixture, and extracted with AcOEt. The extract was washed with water, dried and evaporated to dryness. Recrystallization from $CHCl_3$ yielded orange plates, 60 mg, m.p. 125°. (Found: C, 62·09; H, 6·55; OMe, 6·67. $C_{24}H_{30}O_9$ requires: C, 62·32; H, 6·54; OMe, 6·70%.) ν_{max}^{Nujol} 3400, 1650, 1600 cm^{-1}.

Isopropylidenechromomyciquinone tetraacetate **25**

Compound **24** (100 mg) was dissolved in a mixture of pyridine (2 ml) and acetic anhydride (1 ml). The reaction mixture was set aside at room temp overnight, and poured into ice-water. Recrystallization of the precipitate from EtOH yielded yellow needles, (90 mg), m.p. 176°. (Found: C, 60·65; H, 6·03; OAc, 26·66. $C_{32}H_{38}O_{13}$ requires: C, 60·95; H, 6·03; OAc, 27·30%.) λ_{max}^{EtOH} (log ε) 258 mμ (4·40), 275 (4·02), 351 (3·57). $\nu_{max}^{CHCl_3}$ 1775, 1735, 1670, 1600 cm^{-1}. NMR.[8]

Isochromomycinone **(29)**

Compound **1** (3 g) was dissolved in 8% K_2CO_3aq (100 ml) and the solution was left to stand at room temp for 4 hr. After neutralizing with oxalic acid, the reaction mixture was extracted with AcOEt, and the organic extract was washed, and evaporated to dryness. The residue, after recrystallization from acetone, afforded yellow platelets, m.p. 227° (dec.); yield 2·3 g. (Found: C, 58·69; H, 5·83; OMe, 7·20. $C_{21}H_{24}O_9 \cdot \frac{1}{2}H_2O$ requires: C, 58·74; H, 5·82; OMe, 7·22%.) λ_{max}^{EtOH} (log ε) 232 mμ (4·36), 282 (4·55), 328 (3·83), 341 (3·84), 418 (3·98). ν_{max}^{KBr} 3400, 1635, 1610, 1580 cm^{-1}.

Isochromomycinone pentaacetate **(30)**

Compound **29** (1 g) was dissolved in pyridine (3 ml) and acetic anhydride (1·5 ml) and the solution was left to stand at room temp for 3 days. The mixture was then poured into ice-water and insoluble material was collected, washed with water and dried. After chromatography on silica gel a single product was obtained, yield 500 mg. (Found: C, 59·04; H, 5·36; OMe, 4·67. $C_{31}H_{34}O_{14}$ requires: C, 59·04; H, 5·39; OMe, 4·92%.) λ_{max}^{EtOH} (log ε) 260 mμ (4·73), 302 (3·83), 366 (3·43). $\nu_{max}^{CCl_4}$ 3400,

1780, 1750, 1700, 1630, 1610 cm^{-1}. NMR ($CDCl_3$) δ 1·38 (3H, d, J 6·5), 2·09 (9H, s), 2·34 (3H, s) 2·41 (3H, s), 2·49 (3H, s), 3·48 (3H, s), 3·63 (1H, t, J 9), 4·41 (1H, d, J 12), 4·97 (1H, q, J 6·5), 5·15 (1H, d, J 9·5), 7·33 (1H, s), 7·43 (1H, s).

Isopropylideneisochromomycinone (**31**)

A solution of **29** (500 mg) in acetone (20 ml) and a drop of H_2SO_4 was allowed to stand at room temp for 2 hr. The mixture was then poured into ice-water, extracted with AcOEt and the organic extract was washed, dried and evaporated. Chromatography of the residue on silica gel furnished a single crystalline substance, which melted at 226° (dec.), yield 400 mg. (Found: C, 62·75; H, 6·20. $C_{34}H_{38}O_9$ requires: C, 62·60; H, 6·13%.) $\nu_{max}^{CHCl_3}$ 3500, 3325, 1620, 1575 cm^{-1}.

Isopropylideneisochromomycinone triacetate **32**

Compound **31** (400 mg) was dissolved in pyridine (2 ml) and acetic anhydride (2 ml). The mixture was heated at 70–80° on a water bath for 2 hr, poured into ice-water, and extracted with AcOEt. The extract was washed, dried and evaporated to dryness under red. press. The resulting residue was dissolved in $CHCl_3$, and purified by chromatography on silica gel treated with 1% oxalic acid. The chromatogram was eluted with $CHCl_3$, and the eluate was evaporated to dryness to afford 200 mg of an amorphous solid which showed a single spot on TLC. (Found: C, 59·59; H, 5·62; OMe (1), 5·24. $C_{30}H_{34}O_{12}\cdot H_2O$ requires: C, 59·60; H, 5·96; OMe 5·13%.) λ_{max}^{EtOH} (log ε) 226 mμ (4·48), 263 (sh), 272 (4·62), 293 (3·89), 3·04 (3·91), 390 (3·76). $\nu_{max}^{CHCl_3}$ 3500, 1765, 1755 (sh), 1630, 1570 cm^{-1}. NMR ($CDCl_3$) δ 1·24 (3H, d, J 6·3), 1·53 (6H, s, gem-dimethyl), 2·11 (3H, s, arom Me), 2·13 (3H, s, OAc), 2·34 (3H, s, OAc), 2·38 (3H, s, OAc), 3·50 (3H, s, OMe), 3·58 (1H, t, J 9·1), 4·49 (1H, q, J 6·3), 4·53 (1H, d, J 12·1), 5·04 (1H, d, J 9·1), 6·97 (1H, s, arom H), 7·27 (1H, s, arom H), 14·40 (1H, s, —OH).

Isopropylideneisochromomycinone tetraacetate **33**

Compound **31** (200 mg) was dissolved in pyridine (2 ml) and acetic anhydride (2 ml) and set aside for 4 days at room temp. The reaction mixture was poured into ice-water, extracted with AcOEt, and the extract was washed, dried and evaporated to dryness. The resulting residue was dissolved in $CHCl_3$, and chromatographed on silica gel pre-treated with 1% oxalic acid. The chromatogram was eluted with $CHCl_3$ and the eluate was evaporated to dryness to give 100 mg of solid. (Found: C, 61·42; H, 5·69; OMe, 4·98. $C_{38}H_{46}O_{13}$ requires: C, 61·14; H, 5·73; OMe, 4·93%.) λ_{max}^{EtOH} (log ε) 260 mμ (4·78), 302 (3·91), 362 (3·45). $\nu_{max}^{CCl_4}$ 1780, 1750, 1700, 1630, 1610 cm^{-1}. NMR ($CDCl_3$) δ 1·24 (3H, d, J 6·5), 1·51 (6H, s), 2·08 (3H, s, arom Me), 2·13 (3H, s), 2·34 (3H, s), 2·40 (3H, s), 2·48 (3H, s), 3·47 (3H, s), 3·61 (1H, t, J 9·0), 4·49 (1H, d, J 12), 4·49 (1H, q, J 6·5), 5·01 (1H, d, J 9), 7·40 (1H, s), 7·51 (1H, s).

1-*Deoxoisochromomycinone* (**34**)

(a) *From* **29**. Compound **29** (900 mg) dissolved in EtOH (90 ml) was hydrogenated over Pt catalyst. After uptake of 2 moles of H_2 during a period of 7 hr, the catalyst was filtered and the filtrate was evaporated to yield pale yellow crystals (800 mg). Recryatallization from EtOH furnished platelets, m.p. 230° (dec.). (Found: C, 61·74; H, 6·47; OMe, 7·61. $C_{31}H_{36}O_8$ requires: C, 62·06; H, 6·45; OMe, 7·63%.) λ_{max}^{EtOH} (log ε) 244 mμ (4·42), 297 (3·44), 342 (3·59). ν_{max}^{KBr} 3300, 1650, 1620, 1590 cm^{-1}.

(b) *From* **18**. Treatment of **18** with 8% K_2CO_3 and working up as described in the case of the preparation of **29** afforded in a good yield compd **34**, which was identical in all respects with the specimen obtained in (a).

Isopropylidene-1-deoxoisochromomycinone tetraacetate **35**

Compound **34** (500 mg) was treated with acetone and a small quantity of H_2SO_4, and the resulting isopropylidene derivative was acetylated with acetic anhydride and pyridine. After the usual working up, followed by chromatography, the acetate **35** was obtained as a non-crystalline powder; yield 416 mg. (Found: C, 62·27; H, 6·10; OMe, 5·06; $C_{38}H_{46}O_{12}$ requires: C, 62·53; H, 6·23; OMe, 5·04%.) λ_{max}^{EtOH} (log ε) 235 mμ (5·08), 283 (3·75), 292 (3·75). $\nu_{max}^{CHCl_3}$ 1760, 1370, 1230, 1200, 1080 cm^{-1}. NMR ($CDCl_3$) δ 1·26 (3H, d, J 6·5), 1·52 (6H, s), 2·10 (3H, s), 2·15 (3H, s), 2·34 (3H, s),

2·40 (3H, s), 2·42 (3H, s), 3·49 (3H, s), 3·67 (1H, t, J 9·2), 4·28 (1H, q, J 6·5), 5·07 (1H, d, J 9·2), 7·41 (1H, s), 7·49 (1H, s).

3′-Dehydrochromomyciquinone (**36**)

(a) A solution of **34** (1 g) in 10% K_2CO_3aq (30 ml) placed in a Petri dish was exposed to the air for 48 hr. During this period the reaction mixture turned to a dark red solution, which was neutralized with oxalic acid, and extracted with AcOEt. The extract was washed, dried, and the residue was recrystallized from AcOEt to yield 750 mg of crystals, m.p. 223° (dec.). (Found: C, 60·07; H, 5·80; OMe, 7·44. $C_{31}H_{34}O_9$ requires: C, 60·00; H, 5·71; OMe, 7·38%.) λ_{max}^{EtOH} (log ε) 256 mμ (4·27), 300 (4·06), 415 (3·70). ν_{max}^{KBr} 3400, 1650, 1600 cm^{-1}.

(b) Similar treatment of **18** also yielded **36**.

3′-Dehydrochromomyciquinone tetraacetate **37**

Compound **36** (200 mg) was acetylated with acetic anhydride and pyridine. The reaction mixture, after working up by the usual method, was chromatographed over silica gel. A yellow non-crystalline substance, which gave a single spot on TLC, was isolated; yield 100 mg. (Found: C, 59·00; H, 5·50; OMe, 5·36. $C_{39}H_{42}O_{13}$ requires: C, 59·18; H, 5·44; OMe, 5·27%.) λ_{max}^{EtOH} (log ε) 260 mμ (4·37), 276 (4·10), 352 (3·56). $\nu_{max}^{CCl_4}$ 3500, 1780, 1750, 1680, 1670, 1600 cm^{-1}. NMR ($CDCl_3$) δ 1·30 (3H, d, J 6·5), 2·00 (3H, s), 2·05 (3H, s), 2·10 (3H, s), 2·36 (3H, s), 2·44 (3H, s), 3·47 (3H, s), 3·75 (1H, s), 4·86 (1H, q, J 6·5), 5·20 (1H, d, J 9·5), 7·80 (1H, s).

Isopropylidene-3′-dehydrochromomyciquinone triacetate **38**

To a suspension of **36** (300 mg) in acetone (10 ml) was added a drop of H_2SO_4, and the mixture was stirred for 2 hr. The solvent was removed under red. press. and the residue was taken up in AcOEt. After washing, drying and evaporation, the residue was chromatographed on silica gell to yield a single noncrystalline powder; yield 200 mg. (Found: C, 60·42; H, 6·00; OMe, 6·76. $C_{34}H_{36}O_9 \cdot H_2O$ requires: C, 60·25; H, 6·07; OMe, 6·48%.) λ_{max}^{EtOH} (log ε) 256 mμ (4·26), 299 (4·05), 415 (3·67). $\nu_{max}^{CHCl_3}$ 3500, 3350, 1650, 1610 cm^{-1}.

The isopropylidene compound thus obtained was acetylated with acetic anhydride and pyridine, and the reaction mixture, after the usual work up, was chromatographed on silica gel to yield 100 mg of the acetate **38**. (Found: C, 60·96; H, 5·76; OMe, 5·35. $C_{30}H_{34}O_{13}$ requires: C, 61·43; H, 5·80; OMe, 5·29%.) λ_{max}^{EtOH} (log ε) 259 mμ (4·36), 275 (4·09), 352 (3·54). $\nu_{max}^{CCl_4}$ 1780, 1750, 1680, 1670, 1600 cm^{-1}. NMR ($CDCl_3$) δ 1·26 (3H, d, J 6·5), 1·55 (6H, s), 2·05 (3H, s), 2·17 (3H, s), 2·41 (3H, s), 2·51 (3H, s), 3·51 (3H, s), 3·66 (1H, t, J 9·5), 4·30 (1H, q, J 6·5), 5·06 (1H, d, J 9·5), 7·85 (1H, s).

3′-Dehydrochromomyciquinone methyl ketal **39**

Compound **36** (600 mg) dissolved in 5% methanolic HCl (60 ml) was refluxed for 5–10 min. After removal of a small quantity of insoluble material by filtration, the filtrate was set aside at room temp to yield yellow needles; m.p. 153° (dec.); yield 500 mg. (Found: C, 58·50; H, 6·15; OMe, 14·07. $C_{32}H_{36}O_9 \cdot H_2O$ requires: C, 58·40; H, 6·19; OMe, 13·71%.) λ_{max}^{EtOH} (log ε) 256 mμ (4·24), 299 (4·04), 415 (3·66). ν_{max}^{KBr} 3350, 1650, 1600 cm^{-1}. NMR (pyridine) δ 1·52 (3H, d, J 6·5), 2·20 (3H, s), 3·52 (3H, s), 3·76 (3H, s).

3′-Dehydrochromomyciquinone methyl ketal tetraacetate **40**

Acetylation of the methyl ketal **39** (300 mg) with acetic anhydride and pyridine followed by recrystallization from EtOH gave pale yellow needles; m.p. 250°; yield 100 mg. (Found: C, 59·55; H, 5·78; OMe, 10·31. $C_{40}H_{44}O_{13}$ requires: C, 59·80; H, 5·64; OMe, 10·29%.) λ_{max}^{EtOH} (log ε) 259 mμ (4·39), 276 (4·13), 352 (3·89). $\nu_{max}^{CHCl_3}$ 1780, 1750, 1680, 1670, 1600 cm^{-1}. NMR ($CDCl_3$) δ 1·36 (3H, d, J 6·5), 2·03 (3H, s), 2·06 (3H, s), 2·18 (3H, s), 2·38 (3H, s), 2·50 (3H, s), 3·28 (3H, s), 3·53 (3H, s), 5·28 (1H, q, J 6·5), 5·30 (1H, d, J 9·5), 7·81 (1H, s).

Similarly treatment of the tetraacetate **37** with 5% MeOH–HCl afforded the methyl ketal tetraacetate **40** which was identical in all respects with the specimen obtained from **39**.

Anhydrochromomycinone enolpentaacetate **41**

Compound **1** (300 mg) dissolved in pyridine (5 ml) and acetic anhydride (5 ml) was left standing overnight, and the mixture was poured into ice-water. After extraction with ether, the ether solution

was washed, dried and evaporated to dryness. Careful chromatography of the mixture on silica gel afforded hexaacetate 7 (100 mg) and 50 mg of an amorphous substance, which could not be induced to crystallize; however, the compd gave a single spot on TLC and the NMR spectrum demonstrated five clear acetoxyl signals and one additional ethylenic proton quartet. (Found: C, 61·01; H, 5·45. $C_{31}H_{38}O_{13}$ requires: C, 60·78; H, 5·22%.) λ_{max}^{EtOH} (log ε) 242 mμ (4·33), 260 (4·82), 360 (3·45). $\nu_{max}^{CHCl_3}$ 1760, 1700, 1630, 1610, 1190 cm^{-1}. NMR ($CDCl_3$) δ 1·80 (3H, d, J 6·5), 2·09 (3H, s), 2·30 (6H, s), 2·36 (3H, s), 2·41 (3H, s), 2·49 (3H, s), 3·30 (3H, s), 4·45 (1H, d, J 2·0), 5·59 (1H, d, J 11·5), 6·60 (1H, q, J 6·5), 7·45 (1H, s), 7·56 (1H, s).

Anhydrochromomycinone-3'-methyl ketal **42**

A solution of **1** (500 mg) in 5% methanolic HCl was left at room temp for 2 days. TLC of the reaction mixture demonstrated that the starting material had disappeared during this period yielding a less polar substance. The reactions mixture was poured into ice-water, extracted with ether, and the organic layer was washed, dried and evaporated. The residue was chromatographed on silica gel to give a single product, which after recrystallization from MeOH afforded yellow needles, m.p. 215°. (Found: C, 63·25; H, 5·86. $C_{32}H_{34}O_8$ requires: C, 63·45; H, 5·76%.) λ_{max}^{EtOH} (log ε) 233 mμ (4·35), 282 (4·57), 342 (3·86), 4·18 (4·01). ν_{max}^{KBr} 3400, 1740, 1625 cm^{-1}.

Anhydrochromomycinone-3'-methyl ketal monoacetate **43**

The methyl ketal **42** (150 mg) and AcONa (150 mg) were dissolved in acetic anhydride (10 ml) and the mixture was heated on a steam bath for 10 min. After cooling the mixture was poured into water, extracted with ether and the ether extract was washed, dried and evaporated. Chromatography of the residue on silica gel with a solvent system of $CHCl_3$–acetone–EtOH (100:3:0·1) furnished the monoacetate **43**. The compd could not be crystallized; however, the amorphous material showed only a single spot on TLC with various solvent systems. (Found: C, 62·68; H, 5·85. $C_{34}H_{36}O_9$ requires: C, 62·88; H, 5·70%.) λ_{max}^{EtOH} (log ε) 225 mμ (4·42), 273 (4·66), 415 (3·92). $\nu_{max}^{CHCl_3}$ 3400, 1755, 1635, 1590 cm^{-1}. NMR ($CDCl_3$) δ 1·00 (3H, t, J 6·5), 1·98 (2H, q, J 6·5), 2·11 (3H, s), 2·34 (3H, s), 3·38 (3H, s), 3·54 (3H, s), 4·23 (1H, d, J 10·0), 4·67 (1H, d, J 12·0), 6·75 (2H, s), 9·94 (1H, s), 15·30 (1H, s).

2-*Deoxychromomycinone pentaacetate* **44**

A solution of chromomycinone hexaacetate (500 mg) in MeOH (5 ml) was treated with a suspension of $(AcO)_2Cr$[16] in MeOH (15 ml), and the mixture was stirred at room temp for 20 min. The reaction mixture was allowed to stand for another 10 min, and then poured into ice-water, and extracted with AcOEt. The extract was washed, dried and evaporated to dryness. The residue (150 mg) was dissolved $CHCl_3$ and chromatographed on silica gel treated with 1% oxalic acid (80 g). The eluate with $CHCl_3$–acetone–EtOH (93:7:1) gave a solid, 50 mg. (Found: C, 60·38; H, 5·67. $C_{31}H_{34}O_{13}$ requires: C, 60·58; H, 5·58%.) λ_{max}^{EtOH} (log ε) 258, 300, 356 mμ. $\nu_{max}^{CHCl_3}$ 1770, 1690, 1640, 1610 cm^{-1}. NMR ($CDCl_3$) δ 1·29 (3H, d, J 6·0), 2·00 (3H, s), 2·10 (3H, s), 2·20 (3H, s), 2·34 (3H, s), 2·42 (3H, s), 2·47 (3H, s), 3·40 (3H, s), 3·83 (1H, d, J 2·0), 5·27 (1H, d, J 2·0), 5·30 (2H), 7·37 (1H, s), 7·45 (1H, s).

Zinc-dust distillation of **1**

A mixture of **1** (100 mg) and Zn dust (1 g) was placed in a round-bottomed flask equipped with a distilling tube. After addition of another 1 g Zn dust, the reaction mixture was heated at 400–500° for 1 hour, during which one drop of oil (5 mg) was distilled. The main constituents were anthracene and 2-methyl anthracene, which were identified with authentic samples by VPC, performed on a Yanagimoto GCG-2 model, with a DEGS column.

Dicarboxylic acid **45** *from* **21**

To a solution of **21** (1 g) in 1% NaOHaq (50 ml), 30% H_2O_2 (20 ml) was added, and the solution was set aside at room temp overnight. The color of the reaction mixture changed from dark brown to red-brown after 7–8 hr and to light blue after 10 hr. A small amount of MnO_2 was added to the reaction mixture to decompose the excess of H_2O_2. It was then passed through a column packed with IR-120. The eluate was condensed to a small volume under red. press. Addition of ether yielded

white powder, 0·6 g m.p. 95–110° (dec.), which gave a single spot on the paper chromatogram (Toyo Roshi No. 51A, 75% phenol–formic acid = 99:1. R_f 0·70–0·73). NMR (D_2O) δ 1·25 (3H, d, J 6·5), 3·41 (3H), 6·92 (1H, s). Preparation of the benzylthiuronium salt by the conventional method yielded needles; m.p. 174° (dec.). (Found: C, 54·46; H, 6·05; N, 7·22; S, 8·33; OMe, 4·55. $C_{33}H_{44}O_{16}N_4S_2 \cdot H_2O$ requires: C, 54·40; H, 6·13; N, 7·46; S, 8·56; OMe, 4·13%.)

Periodate oxidation of **21**

A solution of sodium periodate (100 mg) in water was added to a suspension of **21** (100 mg) in EtOH (10 ml) and AcOEt (5 ml). The reaction mixture was stirred for 5 min at room temp, the inorganic precipitate was filtered and washed with AcOEt, and the filtrate was added to water and extracted with AcOEt. The extract was washed with water, dried and evaporated to dryness. The residue (80 mg) was dissolved in a small amount of pyridine (0·5 ml) and AcOEt (1 ml), and was chromatographed over silica gel (15 g). The chromatogram was eluted with benzene, $CHCl_3$ and then with $CHCl_3$–AcOEt. The first eluate from a 3:2 $CHCl_3$–AcOEt gave a solid (20 mg), which was recrystallized from EtOH to yellow needles, m.p. 201° (dec.). (Found: C, 60·24; H, 5·22. $C_{18}H_{18}O_7 \cdot \frac{1}{2}H_2O$ requires: C, 60·33; H, 5·34%.) ν_{max}^{KBr} 1718, 1667, 1652, 1618 cm^{-1}.

This compd was assigned the structure **46**.

The second eluate from the same mixture yielded a solid (15 mg) on evaporation. Recrystallization from acetone and EtOH afforded needles, m.p. 228–230° (dec.). (Found: C, 62·45; H, 5·46. $C_{18}H_{18}O_7$ requires: C, 62·42: H, 5·24%.) ν_{max}^{KBr} 1660, 1648, 1608 cm^{-1}.

This compd corresponded to the hemiacetal **47**.

Conversion of the aldehyde **46** *to the hemiacetal* **47**

(a) The aldehyde (10 mg) was dissolved in saturated $NaHCO_3$aq (1 ml) and set aside at room temp for 1 day. The reaction mixture was acidified with HCl, and extracted with AcOEt. The extract was washed with water, dried, and evaporated to afford a solid. Recrystallization from hot acetone yielded the hemiacetal **47** in the form of needles.

(b) To a suspension of the aldehyde (15 mg) in EtOH (1 ml) and water (1 ml), two drops of conc. HCl were added. The reaction mixture was refluxed for several hours, and extracted with AcOEt. The extract was washed with water, dried and evaporated to a solid. Recrystallization from hot acetone yielded the hemiacetal **47** as needles.

The methyl derivative **48** *of the hemiacetal* **47**

The hemiacetal **47** (25 mg) was refluxed in 10% methanolic HCl (5 ml) for 3 hr. Crystals appeared upon cooling, which were collected, washed with MeOH and recrystallized from MeOH to afford needles (20 mg), m.p. 211–214°. (Found: C, 63·72; H, 5·62. $C_{19}H_{20}O_7$ requires: C, 63·33; H, 5·35%.) ν_{max}^{KBr} 3450, 1665, 1648, 1610, 1200, 962 cm^{-1}.

The methyl derivative **48** could be reconverted into the hemiacetal **47** by refluxing for 3 hr in 50% AcOH, filtering the reaction mixture, concentrating the filtrate and extracting with AcOEt, evaporating the extract to dryness, and recrystallizing the residue from acetone.

The acetate **49**

The methyl derivative **48** (40 mg) was dissolved in a mixture of pyridine (2 ml) and acetic anhydride (1 ml). The reaction mixture was allowed to stand at room temp for 1 day, and poured into ice-water. Recrystallization from EtOH yielded yellow needles, 30 mg, m.p. 185°. (Found: C, 61·94; H, 5·41. $C_{23}H_{24}O_9$ requires: C, 62·16; H, 5·44%.) ν_{max}^{KBr} 1765, 1740, 1670, 1600 cm^{-1}. NMR ($CDCl_3$) δ 2·03 (3H, s), 2·38 (3H, s), 2·48 (3H, s), 3·47 (6H, s), 5·00 (1H, d, J 2·5), 7·84 (1H, s).

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