The Chemical Conversion of the Photo-dimer of 2-Acetyl-5-methyl-1,4-benzoquinone. The Determination of the Regiochemistry of the Dimer

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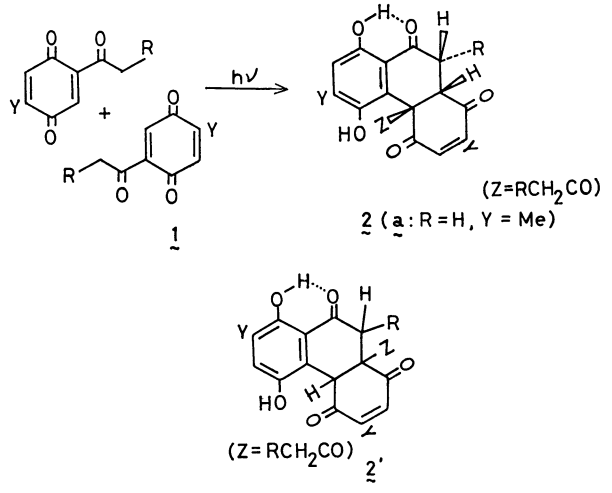
(Received March 21, 1980)

From the photo-dimer (**2a**) of 2-acetyl-5-methyl-1,4-benzoquinone, mono- and diacetyl derivatives and 2,6-dimethyl-1,4,5,8,9-pentaacetoxyphenanthrene (**3**) were prepared. **3** was oxidized to 2,6-dimethyl-1,4,5,8-tetraacetoxy-9,10-phenanthrenequinone (**4**). The acetoxyl groups of **4** were partly deuterated to assign their ^{1}H NMR signals. A series of chemical conversions of **2a** to **4** *via* **3** unambiguously clarified the regiochemistry of **2a**.

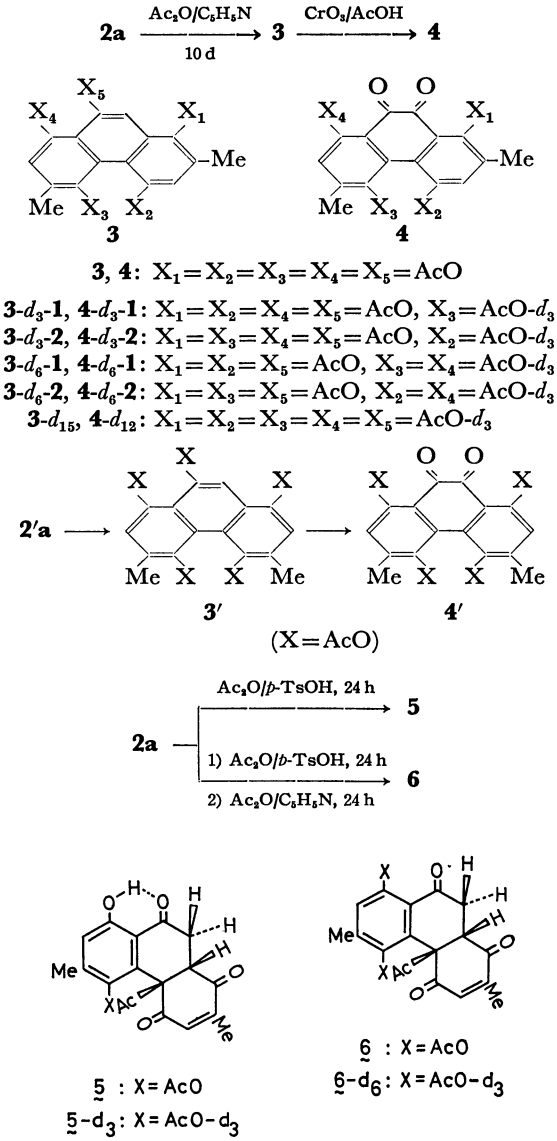
Previously we reported[1] that 2-acyl-1,4-benzoquinones (**1**) underwent a regioselective and stereoselective photo-dimerization to give 4aα-acyl-10β-alkyl-5,8-dihydroxy-4aα,10aα-dihydro-1,4,9(10*H*)-phenanthrenetriones (**2**). Although the structure of **2** was finally established by X-ray structure analysis, its regiochemistry had been determined by a certain sequence of reactions, which converted the dimer of **1a**, (**2a**), to a 9,10-phenanthrenequinone (**4**) through a phenanthrene (**3**).[2] This conversion excluded another possible alternative (**2'**), because **2'a** should give **4'** through **3'**. The series of reactions used in this chemical conversion are unusual and worth to describe. In this paper, the details of these unique and interesting reactions will be given.

On treatment with acetic anhydride containing a crop of *p*-toluenesulfonic acid at room temperature for 24 h, **2a** gave a monoacetyl derivative (**5**).[3] When the solution was further left to stand for 24 h after the addition of a small amount of pyridine, a diacetyl derivative (**6**) was obtained. Their structures were straightforward, judging from their ^{1}H NMR spectra: they were similar to that of **2a** except for the presence of a chelated hydroxyl signal of **5** as well as the lack of hydroxyl signals of **6**.

When a solution of **2a** in Ac_2O–pyridine was left standing over 10 d, 2,6-dimethyl-1,4,5,8,9-pentaacetoxyphenanthrene (**3**) was obtained.[4] Some plausible paths of the reactions are shown in Scheme 1. The structure



1 ; 2 (a: R=H, Y=Me) ; 2'



5 : X=AcO
5-d3: X=AcO-d3

6 : X=AcO
6-d6: X=AcO-d3

of **3** was clarified by its elemental analysis and spectroscopic data. The mass spectrum indicated the presence of five acetoxyl groups. The ^{13}C NMR spectrum was compatible with **3**, showing three doublets and eleven singlets of aromatic carbons (Table 1). The ^{1}H NMR spectrum showed complex signals due to methyl and acetoxyl groups between 2.1 and 2.5, though three singlets due to aromatic protons were observed at 7.12,

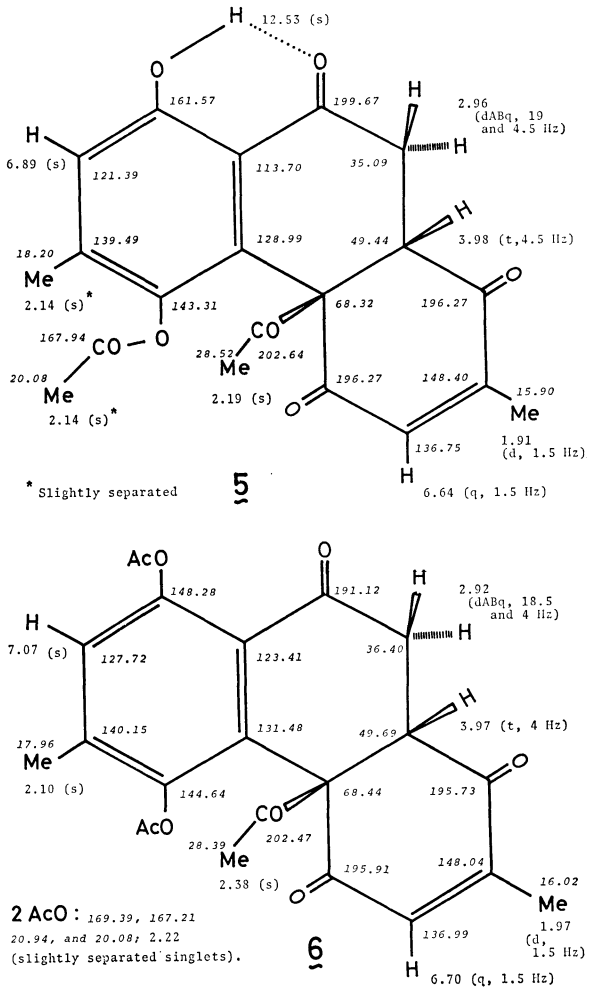
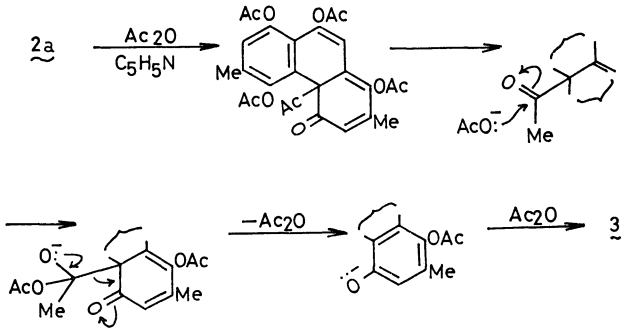


Fig. 1. The ^1H and ^{13}C NMR signals of **5** and **6** in $CDCl_3$ (δ); the ^1H NMR signals of **2a** were shown in Ref. 1; **2a** is not soluble in $CDCl_3$ enough for a ^{13}C NMR measurement and decomposes slowly in acetone.

7.28, and 7.31 in chloroform-*d*. A partially deuterated homologue of **3**, (**3**-d_{15}), was similarly prepared from **2a** with the aid of Ac_2O-d_6. The methyl groups of **3**-d_{15} showed two singlets, at 2.24 and 2.27, in pyridine-d_5; by chance, these singlets arose at the same position (2.30) in chloroform-*d*.

When **3** was oxidized by chromium trioxide, 2,6-dimethyl-1,4,5,8-tetraacetoxy-9,10-phenanthrenequinon (**4**) was obtained. Its ^{13}C NMR spectrum showed two



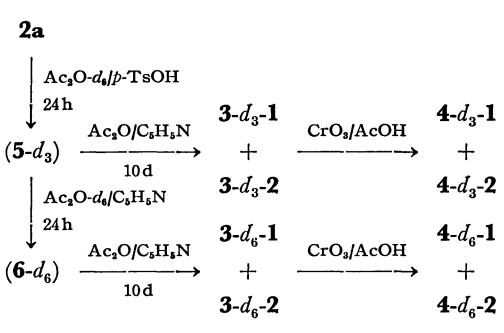
Scheme 1.

Table 1. Carbon chemical shifts in $CDCl_3$ δ

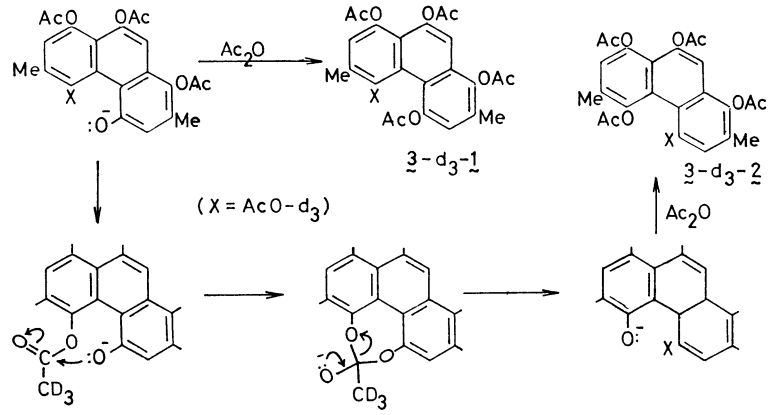
	3	**4**
$\underline{C}H_3$	16.55, 16.88	16.11, 17.74
$\underline{C}H_3CO_2$	20.45, 21.10	20.34, 20.67, 21.32
C-3, C-7, and C-10	112.97, 118.83, 120.28, 123.04, 124.34	120.60, 122.39, 125.32, 126.79 (C-1, C-2, C-4, C-5, C-6, and C-8)
C-1, C-2, C-4, C-5, C-6, C-8, and C-9	124.99, 126.77, 128.23, 129.86, 130.51	128.58, 129.39, 132.97, 135.25 (C-3 and C-7)
C-4a, C-4b, C-8a, and C-10a	141.22, 142.36, 143.98, 144.95	142.25, 144.69, 146.80, 148.43
$CH_3\underline{C}O_2$	167.85, 168.33, 168.98	168.13, 169.27, 170.08
		180.33, 181.31 (C-9 and C-10)

doublets and ten singlets of aromatic carbons and two singlets of quinonoid carbonyl carbons (Table 1).

The ^1H NMR spectrum of **4** in chloroform-*d* showed two singlets[5] due to the aromatic protons at 7.08 and 7.48. In addition, it showed three singlets due to four acetoxyl groups at 2.16, 2.30, and 2.42, and two slightly split singlets due to two methyl groups at 2.27, with the relative-intensity ratio of 1 : 1 : 2 : 2. This assignment was made by a comparison of the spectrum with that of a partially deuterated homologue of **4**, (**4**-d_{12}), which was similarly prepared from **3**-d_{15}; the methyl signals of **4**-d_{12} arose clearly separated at 2.15 and 2.22 in pyridine-d_5. To assign the three singlets at 2.16, 2.30, and 2.42 to the individual acetoxyl groups, partial deuterium labellings of the acetoxyl groups of **4** were undertaken (Scheme 2).



Scheme 2.



Scheme 3.

At first, after letting a solution of **2a** in Ac_2O-d_6–*p*-TsOH stand for 24 h, the concentrated residue[6] (the main component, **5**-d_3) was further treated with Ac_2O–pyridine for 10 d. At this stage, the scrambling of the CD_3CO group between the C-4 and C-5 positions was expected to give a mixture of **3**-d_3-**1** and **3**-d_3-**2**, as is shown in Scheme 3. The mixture thus obtained was oxidized by chromium trioxide to give a mixture of **4**-d_3-**1** and **4**-d_3-**2**, which showed a ^{1}H NMR spectrum in chloroform-*d* identical with that of **4**, with the exception of the decreased intensities of the signals at 2.16 and 2.30. Consequently, these two signals were ascribed to the acetoxyl groups at the C-4 and C-5 positions of **4**.

Secondly, after letting a solution of **2a** in Ac_2O-d_6–*p*-TsOH stand for 48 h, while meanwhile adding a small amount of pyridine, the concentrated residue[6] of the solution (the main component, **6**-d_6) was treated again with Ac_2O–pyridine for 10 d. A scrambling of the CD_3CO group similar to that described above was expected to give a mixture[7] of **3**-d_6-**1** and **3**-d_6-**2**, which was also oxidized to a mixture of **4**-d_6-**1** and **4**-d_6-**2**. The ^{1}H NMR spectrum of the mixture in chloroform-*d* showed the signals at 2.16, 2.30, and 2.42 with decreased intensities. Accordingly, the signal at 2.42 was assignable to two acetoxyl groups at the C-1 and C-8 positions of **4**.

The above spectroscopic studies excluded the reaction sequence of **2'a**→**3'**→**4'**, for the ^{13}C and ^{1}H NMR spectra obtained for **4** were inconsistent with **4'**; **4'** should show a doublet and five singlets of the aromatic carbons and a singlet of the quinonoid carbonyl carbons because of its molecular symmetry, while the ^{1}H NMR spectrum should give a singlet due to the methyl groups, two due to the acetoxyl groups, and one due to the aromatic protons.

Experimental

The Monoacetyl Derivative of ***2a****, 5-Acetoxy-4aα-acetyl-2,6-dimethyl-8-hydroxy-4aα,10aα-dihydro-1,4,9(10H)-phenanthrenetrione (5).* A homogeneous solution was made by occasionally swirling a suspension of **2a** (0.5 g) in acetic anhydride (30 ml) containing a crop of *p*-toluenesulfonic acid. After the solution had stood for 24 h, the solvent was evaporated by bulb-to-bulb distillation through a vacuum-line. The syrupy residue became a semi-solid on standing overnight. After rinsing with benzene, the solid was dissolved in a minimum amount of chloroform. After the addition of petroleum ether, the solution was stored in a refrigerator. Colorless crystals obtained in 10—30% yields gradually melted at 110—130 °C in a vacuum-sealed capillary. Found: C, 64.57; H, 4.66%. Calcd for $C_{20}H_{18}O_7$: C, 64.86; H, 4.90%. MS: *m/e* 370 (M^+), 328, 286.

The Diacetyl Derivative of ***2a****, 4aα-Acetyl-5,8-diacetoxy-2,6-dimethyl-4aα,10aα-dihydro-1,4,9(10H)-phenanthrenetrione (6).* After the above solution of **2a** in Ac_2O–*p*-TsOH had stood for 24 h, the solution was left further to stand for 24 h with the addition of pyridine (0.5 ml). Colorless crystals were thereafter obtained in 10—30% yields by the same procedure as above. They melted at 110—130 °C in a vacuum-sealed capillary. Found: C, 63.84; H, 4.76%. Calcd for $C_{22}H_{20}O_8$: C, 64.07; H, 4.89%. MS: *m/e* 412 (M^+), 370, 328, 286.

2,6-Dimethyl-1,4,5,8,9-pentaacetoxyphenanthrene (3). The above solution of **2a** in Ac_2O–pyridine was left standing for 10 d. The solvent was then evaporated by bulb-to-bulb distillation through a vacuum-line. The black semi-solid residue was rinsed with benzene and purified by column chromatography on silica gel ($10\phi \times 100$ mm; petroleum ether–diethyl ether (1 : 1)). Colorless crystals obtained in 20—40% yields were rectystallized from acetone. Mp 233—234 °C. Found: C, 62.78; H, 4.86%. Calcd for $C_{26}H_{24}O_{10}$: C, 62.90; H, 4.87%. MS: *m/e* 496 (M^+), 454, 412, 370, 328, 286. ^{1}H NMR: δ ($CDCl_3$) 2.18 (3H, s, AcO), 2.32 (6H, two slightly split s, 2 Me), 2.37 (9H, m, 3 AcO), 2.44 (3H, s, AcO), 7.12 (1H, s, ArH), 7.18 (1H, s, ArH), 7.32 (1H, s, ArH).

2,6-Dimethyl-1,4,5,8-tetraacetoxy-9,10-phenanthrenequinone (4). **3** (0.3 g) was dissolved in acetic acid (10 ml) by slight warming. CrO_3 (0.5 g) was dissolved in a minimum amount of water and diluted with acetic acid (5 ml). The CrO_3 solution was added dropwise to the solution of **3** over 1 h at 15 °C. After stirring for an additional hour, the solution was poured into water. The product was immediately extracted with choroform, washed, dried, and concentrated. The solid residue was dissolved in benzene (30 ml), while an amorphous solid remained undissolved. The yellow supernatant was concentrated to a solid, which was dissolved again in benzene. The yellow crystals obtained by repeating this procedure were rinsed with dry acetone and then washed with hot ligroine. Yield, 20—30%; mp 259—264 °C (in a vacuum-sealed capillary; softening, 240 °C). Recrystallization from hot solvents was unsuccessful because of decomposition. Found: C, 61.29; H, 4.15%. Calcd for $C_{24}H_{20}O_{10}$: C, 61.54; H, 4.30%. MS: *m/e* 468 (M^+), 426, 384, 342, 300. ^{1}H NMR:

δ ($CDCl_3$) 2.16 (3H, s, AcO), 2.27 (6H, slightly separated s, 2 Me), 2.30 (3H, s, AcO), 2.42 (6H, s, 2 AcO), 7.08 (1H, s,[5] ArH), 7.48 (1H, s,[5] ArH); δ (pyridine-d_5) 2.15 (6H, s, AcO and Me), 2.22 (3H, d, J=0.7 Hz, Me), 2.32 (3H, s, AcO), 2.38 (6H, s, 2 AcO), 7.68 (1H, s,[5] ArH[8]).

2,6-Dimethyl-1,4,5,8,9-penta(acetoxy-d_3)phenantherene (3-d_{15}). It was prepared from **2a** using Ac_2O-d_6 by the same method as that used for **3**, and it gave satisfactory results in mass analysis; ^{1}H NMR: δ ($CDCl_3$) 2.30 (6H, s, 2 Me), 7.09 (1H, s, ArH), 7.15 (1H, s, ArH), 7.30 (1H, s, ArH); δ (pyridine-d_5) 2.24 (3H, s, Me), 2.27 (3H, s, Me), 7.36 (1H, s, ArH), 7.52 (1H, s, ArH[8]).

2,6-Dimethyl-1,4,5,8-tetra(acetoxy-d_3)-9,10-phenanthrenequinone (4-d_{12}). It was prepared from **3**-d_{15} by the same method as that used for **4**, and it gave satisfactory results in mass analysis; ^{1}H NMR: δ ($CDCl_3$) 2.27 (6H, s, 2 Me), 7.04 (1H, s,[5] ArH), 7.48 (1H, s,[5] ArH); δ (pyridine-d_5) 2.15 (3H, s, Me), 2.22 (1H, s, Me), 7.70 (1H, s, ArH[8]).

The Partially Deuterated Homologues of 3 and 4, (3-d_3-1+3-d_3-2), (3-d_6-1+3-d_6-2), (4-d_3-1+4-d_3-2), and (4-d_6-1+4-d_6-2). These were prepared by the method described in the preceding section.

NMR measurements were made with a JEOL JNM-PS 100 spectrometer. We wish to thank Dr. Y. Itatani, Faculty of Pharmaceutical Sciences, Kanazawa University, for the NMR measurements and for his valuable discussions.

References

1) Y. Miyagi, K. Maruyama, H. Ishii, S. Mizuno, M. Kakudo, N. Tanaka, Y. Matsuura, and S. Harada, *Bull. Chem. Soc. Jpn.*, **52**, 3019 (1979).

2) Y. Miyagi, K. Kitamura, K. Maruyama, and Y. L. Chow, *Chem. Lett.*, **1978**, 33.

3) By the same procedure, **2** (R=Me, Y=Cl) gave the monoacetyl derivative corresponding to **5**.[1]

4) Similarly, 1,4,5,8,9-pentaacetoxyphenanthrene (mp 192—194.5 °C) and 10-methyl-1,4,5,8,9-pentaacetoxyphenanthrene (mp 190—193 °C) were obtained from **2** (R=Y=H) and **2** (R=Me, Y=H) respectively. The mass spectroscopic analysis of the latter phenenthrene indicated the contamination with methyl(propanoyloxy)tetraacetoxyphenanthrene, which supports the reaction mechanism of Scheme 1: acetic propionic anhydride and a phenanthrolate are formed by the Retro-Cleisen condensation, and the reaction between them gives the third phenanthrene and an acetate anion.

5) They seemed to be quartets in expanded measurements.

6) Because the isolation of the partially deuterated products (**3**-d_3 and **4**-d_6) in each step did not produce yields good enough to obtain the final products, the concentrated residue was submitted to further reactions. The evaporation of the solvent was effected by bulb-to-bulb distillation through a vacuum-line.

7) The complex signals of **3** at 2.37 did not become enough simpler to assign them to the individual acetoxyl groups by deuteration.

8) The signal of another aromatic proton might be behind the signals of the residual protons of pyridine.