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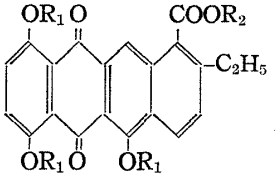
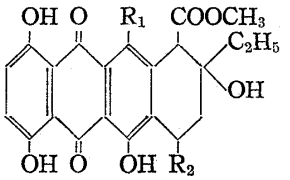
Conversion of Methyl 2-Ethyl-6,11-dihydro-6,11-dioxo-5,7,10-trimethoxy-1-naphthacenecarboxylate into η-Pyrromycinone

In the preceding communication[1] were reported the synthesis of methyl 2-ethyl-6,11-dihydro-6,11-dioxo-5,7,10-trimethoxy-1-naphthacenecarboxylate (I) and the demethylation of I to η-pyrromycinonic acid (II). Later, we re-examined this demethylation and found that it gave η-pyrromycinone (III) as well. The present paper describes the identification of synthetic I, II, and III with natural η-pyrromycinone trimethyl ether, η-pyrromycinonic acid and η-pyrromycinone, respectively.



I : $R_1=R_2=CH_3$
II : $R_1=R_2=H$
III : $R_1=H$, $R_2=CH_3$



IV : $R_1=H$, $R_2=OH$
V : $R_1=R_2=H$
VI : $R_1=R_2=OH$
VII : $R_1=OH$, $R_2=H$

Natural I (bright yellow needles from methanol, m.p. 235~237°) was prepared by refluxing natural II with methyl iodide in dry acetone in the presence of anhydrous potassium carbonate, and was identified with synthetic I, by comparison of their infrared spectra (KBr) and mixed melting point determination.

Demethylation of synthetic I was carried out by the method reported previously,[1] that is, with a large excess of boron tribromide in dry methylene chloride at room temperature, giving bright red needles of III, m.p. 238~239° (IR ν_{max}^{KBr} cm^{-1} : 1724, 1644), as a neutral fraction and dark red needles of II, m.p. 260~262° (decomp.) (IR ν_{max}^{KBr} cm^{-1}: 1704, 1648, 1600, 1587), as an acidic fraction. The former was identified with natural III[2,3] and the latter with natural II[2] by comparison of their infrared spectra (KBr).

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The results confirm the structure of η-pyrromycinone (Ⅲ) and also the carbon skeletons of ε-pyrromycinone (Ⅳ),[4] ζ-pyrromycinone (Ⅴ),[4] ε-isorhodomycinone (Ⅵ)[5] and ζ-isorhodomycinone (Ⅶ),[5] since these anthracyclinones have been related to Ⅲ.

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Gas Chromatography of Aromatic Acids

Gas chromatographic separation of aromatic acids usually requires conversion of the acids to suitable volatile derivatives. This has been carried out by treating the acids with diazomethane, and thus, a number of methyl esters of aromatic acids have been chromatographed satisfactorily.[1,2] However, the application of this method to determination of acids with two phenolic hydroxyl groups such as protocatechuic acid was unsuccessful because of the conversion by diazomethane to a mixture of derivatives.[2] In order to solve this problem, an improved method[3] which involves acetylation of phenolic groups, followed by methylation, has been devised, but the method is tedious and time consuming.

We have now developed a rapid and convenient method which is widely applicable to separation and determination of a variety of aromatic acids including phenolic acids. This development has stemmed from our recent finding[4] that carboxylic acids can be readily and quantitatively converted to their trimethylsilyl (TMS) esters by the use of the convenient silylation procedure.[5,6]

The aromatic acids were converted to their TMS derivatives in the following manner: 1~5 mg. of the acid was placed into a small stoppered vial and dissolved in 0.8 ml. of dry pyridine. To this solution was added 0.1 ml. of trimethylchlorosilane, followed by 0.1 ml. of hexamethyldisilazane. The reaction sequence may be written as follows:

$$R\begin{matrix}COOH\\(OH)\end{matrix} + (CH_3)_3Si\text{-}Py^+Cl^- \rightleftarrows R\begin{matrix}COOSi(CH_3)_3\\(OSi(CH_3)_3)\end{matrix} + Py\cdot HCl$$

$$Py\cdot HCl + (CH_3)_3SiNHSi(CH_3)_3 \longrightarrow (CH_3)_3Si\text{-}Py^+Cl^- + NH_4Cl \downarrow$$

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