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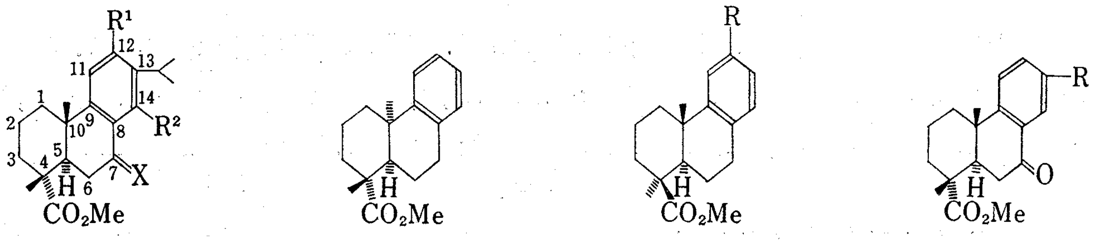
Novel Nitration Reaction of Methyl 7-Oxodehydroabietate

In dehydroabietic acid type compounds, many substitution reaction have been reported. In general, nitration gave a mixture of positional isomers (*e.g.* methyl dehydroabietate (I)→12-nitro (II) and 14-nitro esters (III)[1] and methyl deisopropyl-*allo*-dehydroabietate (IV)→12-, 13-, and 14-nitro compounds[2]) and, on the contrary, acetylation only afforded 12-substituted compound (*e.g.* I→V[3] and methyl deoxypodocarpate (VI)→VII[4]). Selective substitution at 13-position was accomplished by nitration of 7-oxo compound (*e.g.* VIII→IX[5]).

From the above experimental facts, nitration of methyl 7-oxodehydroabietate[6] (X) aroused our interest. The reason is that the C-11 and C-13 positions to the polar 7-oxo group in 7-oxo ester (X) are sterically hindered and are substituted by an isopropyl group, respectively.

Nitration of X under the usual nitration condition (fuming HNO_3–conc. H_2SO_4 (10: 1), 0—5°) gave crystals (*ca.* 95% yield) as a neutral part, whose gas–liquid chromatogram (GLC) showed that it consisted of two components in 1: 1 ratio. The crystals were purified by careful chromatography on deactivated neutral alumina and subsequent recrystallization gave XI, mp 187—189°, and IX, mp 155.5—156.5°. The two crystalline products were identified with authentic 14-nitro-7-oxo ester[7] (XI) and 13-nitro-7-oxo ester[5] (IX) by comparison of their physical constants (mixed mp, infrared, nuclear magnetic resonance and GLC). It is notable that 14-nitration (XI) at the position *ortho* to the 7-oxo group and 13-nitro-dealkylation (IX) had occurred. In spite of the possibility of a nitration at 11- or 12-position, it is interesting that the nitration took place preferentially at 14-position.



I: $R^1=R^2=H$, $X=H_2$
II: $R^1=NO_2$, $R^2=H$, $X=H_2$
III: $R^1=H$, $R^2=NO_2$, $X=H_2$
V: $R^1=COCH_3$, $R^2=H$, $X=H_2$
X: $R^1=R^2=H$, $X=O$
XI: $R^1=H$, $R^2=NO_2$, $X=O$

IV

VI: $R=H$
VII: $R=COCH_3$

VIII: $R=H$
IX: $R=NO_2$

Fig. 1

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As an analogous nitro-dealkylation, an anomalous nitration (nitro-dealkylation and nitro-deacylation) in polyalkylacyl-benzene series was reviewed,[8] and, recently, Cambie reported that nitration of 12-acetyl ester (V) yields methyl 12,14-dinitrodehydroabietate (nitro-deacylation) and methyl 12-acetyl-13-nitrodeisopropyldehydroabietate (nitro-dealkylation).[3b] However, there is a difference in the relative positions of isopropyl and carbonyl between X (*meta*) and Cambie's substrate (V) (*ortho*). Furthermore, it is interesting that nitro-deacylation type reaction did not occur at C-8 in X.

Application of this nitration reaction to other systems and under different conditions is being examined.

Rikagaku Kenkyusho
(The Institute of Physical
and Chemical Research),
Wako-shi, Saitama-ken

YASUO OHTSUKA
HIROYUKI AKITA
AKIRA TAHARA[9]

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[9] To whom inquiries regarding this communication should be addressed.

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Synthesis of (±)-Fukugetin Heptamethyl Ether

In recent years, new biflavonoids having a carbon-carbon linkage between ring C and ring A' have been found in the heartwood and bark of Guttiferae plants.[1]

Fukugetin is a flavonoid pigment occurring in the bark of *Garcinea spicata* HOOK. f. (Guttiferae). The structure, which has been under investigation for several decades, has recently been shown to be 3-luteolin-(8'')-yl-naringenin (I).[2] We now report the total synthesis of (±)-fukugetin heptamethyl ether (II) for the structure confirmation.

The first step of the synthesis was chloromethylation of 2-hydroxy-4,6-dimethoxyacetophenone (III) with chloromethyl methyl ether in acetic acid to prepare a chloromethylacetophenone derivative (IV), mp 133—135° (decomp.) (57%). The position of the chloromethyl group in IV was established by the fact that palladium charcoal-catalyzed hydrogenolysis of IV gave the known 2-hydroxy-4,6-dimethoxy-3-methylacetophenone (V).[3] IV was converted to a cyanomethyl compound (VI), mp 156—157° and then to a 3,4-dimethoxybenzoylester (VII), mp 202—203°. VII was rearranged with potassium hydroxide in pyridine (Baker–Venkataraman rearrangement) to produce a diketone (VIII), mp 180—182°. Treatment of VIII with sulfuric acid–acetic acid–water afforded 3',4',5,7-tetramethoxyflavon-(8)-yl-acetic acid (IX), mp 276—278° (84%).

Ketoflavone (X), a key intermediate for the synthesis of II, was shown to be obtained conveniently by the Fries rearrangement of a ester (XI), readily obtainable from the flavonylacetic acid (IX) and phloroglucinol dimethyl ether (XII) by means of triphenylphosphine-

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