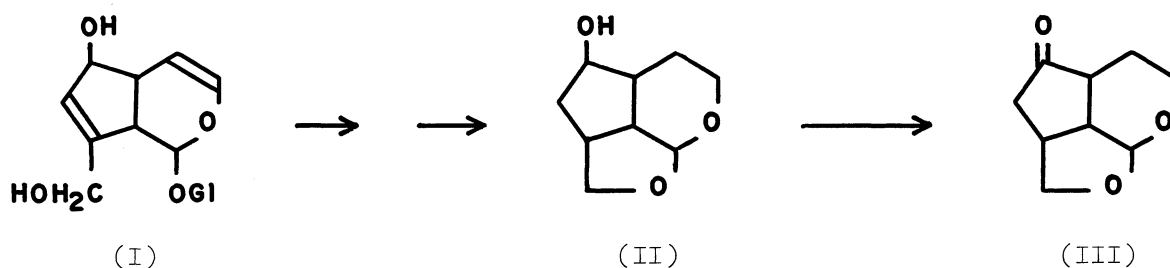


THE SYNTHESIS OF DL-TETRAHYDROANHYDROAUCUBIGENONE

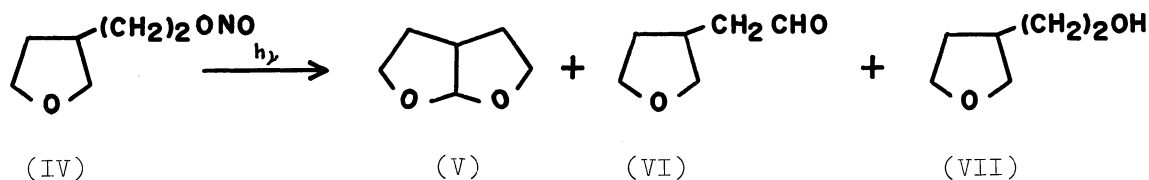
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The racemate of tetrahydroanhydroaucubigenone (III), one of the derivatives of aucubin (I), was synthesized by the photo-irradiation of 2-(2'-nitrosoxyethyl)-7-oxabicyclo [3,3,0] octan-3-one (XV) which was obtained from 2-ethoxycarbonyl-7-oxabicyclo [3,3,0] octan-3-one (VIII) through seven steps.

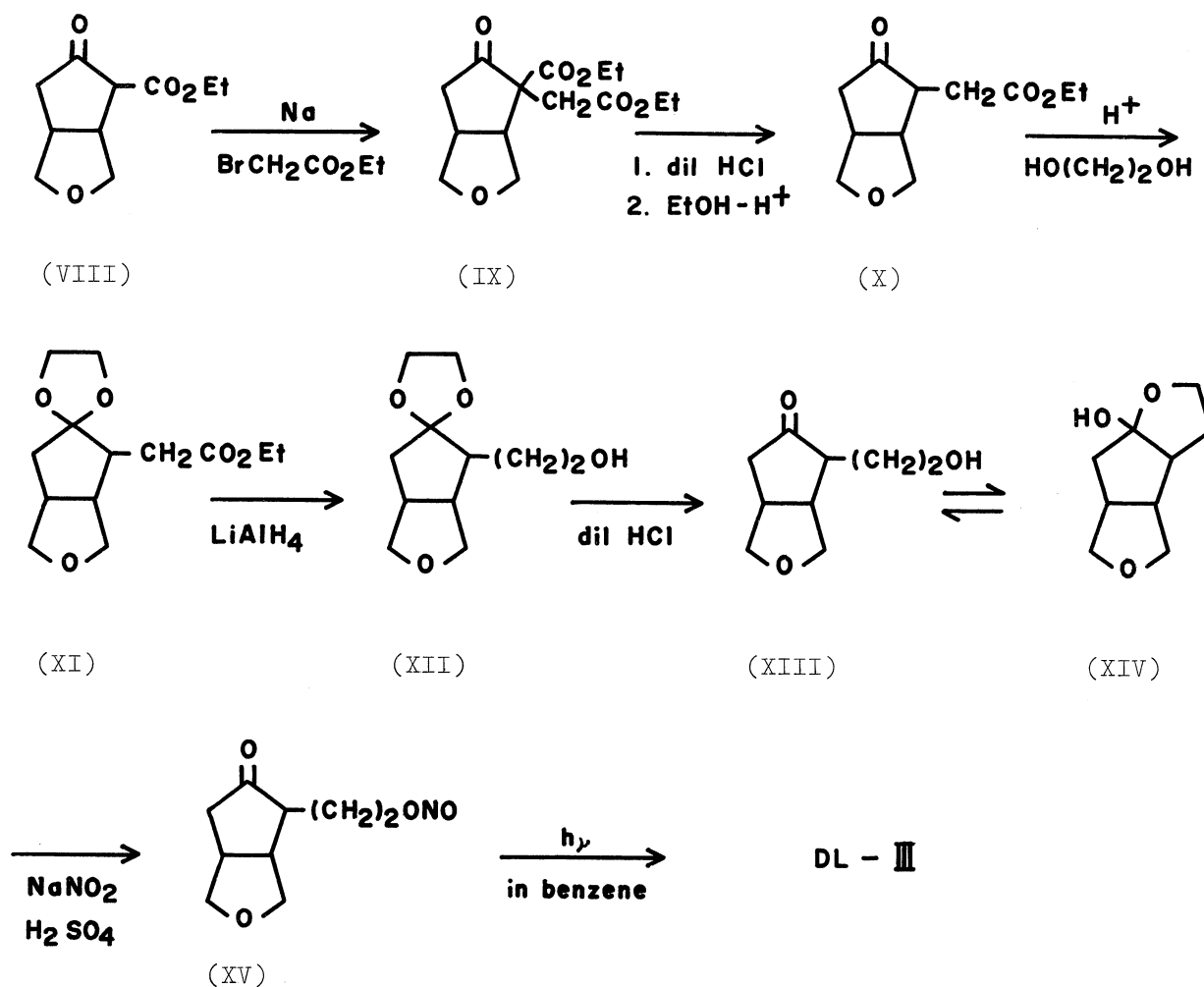
Tetrahydroanhydroaucubigenone (III), mp 77-78°C,  $[\alpha]_D^{17} - 41.3^\circ$  (ethanol), an oxidation product of tetrahydroanhydroaucubigenin (II) which was derived from aucubin (I),<sup>1)</sup> has been first obtained by Fujise<sup>2)</sup> in 1953. The synthesis of III, which is thought to be an important compound for the determination of I, has not been accomplished yet, although some derivatives of I have been obtained.<sup>3)</sup>



Our previous observation that 2,8-dioxabicyclo [3,3,0] octane (V) was prepared by photochemical reaction of 2-(tetrahydrofuryl)ethylnitrite (IV) along with an acetaldehyde derivative (VI) and an ethanol one (VII)<sup>4)</sup> promoted us to investigate this phenomenon in the 7-oxabicyclo [3,3,0] octan-3-one series.



In this communication we wish to describe the photochemical preparation of DL-III by the following scheme.



2-Ethoxycarbonyl-2-ethoxycarbonylmethyl-7-oxabicyclo[3,3,0]octan-3-one (IX), was obtained in a 62% yield with a small amount of O-alkylated compound by the alkylation of the sodio derivative of cis-2-ethoxycarbonyl-7-oxabicyclo[3,3,0]octan-3-one (VIII)<sup>5)</sup> with ethyl bromoacetate in toluene. Hydrolysis and decarboxylation of IX with 6 N hydrochloric acid, followed by esterification, afforded 2-ethoxycarbonylmethyl-7-oxabicyclo[3,3,0]octan-3-one (X) in a 55% yield, bp 129-131°C/2mmHg, 2,4-dinitrophenylhydrazone, mp 144°C. After protection of the carbonyl group of X with ethylene glycol in the presence of *p*-toluenesulfonic acid in benzene, the ethylene-ketal (XI) was reduced into the alcohol (XII) in a 89% yield with lithium aluminium hydride in tetrahydrofuran. Deketalization of XII by treatment with dilute hydrochloric acid, or *p*-toluenesulfonic acid in acetone,

afforded a mixture of 2-(2'-hydroxyethyl)-7-oxabicyclo[3,3,0]octan-3-one (XIII) and its intramolecular hemiketal (XIV) in a 76% yield, 2,4-dinitrophenylhydrazone, mp 154°C. The hemiketal (XIV) is easily converted into keto-alcohol (XIII) by treatment with dilute hydrochloric acid. 2-(2'-Nitrosoxyethyl)-7-oxabicyclo[3,3,0]octan-3-one (XV), bp 100-102°C/2mmHg, a pale green viscous oil, was obtained in a 30% yield from the keto-alcohol (XIII) by treatment with a mixture of sodium nitrite and dilute sulfuric acid.

The irradiation of XV (3g) was carried out in a benzene solution under a nitrogen atmosphere at room temperature for 15 hr using a high-pressure 500 W mercury arc. After irradiation, the benzene was removed in vacuo, and the residue was chromatographed on a column of silica gel with carbontetrachloride-ethyl acetate (3:1) to give DL-III (14mg), colorless prisms, mp 57-57.5°C, (recrystallized from petroleum ether-benzene). The ir (Fig. 1), nmr, and mass spectra of this compound were completely identical with those of the natural sample (III).

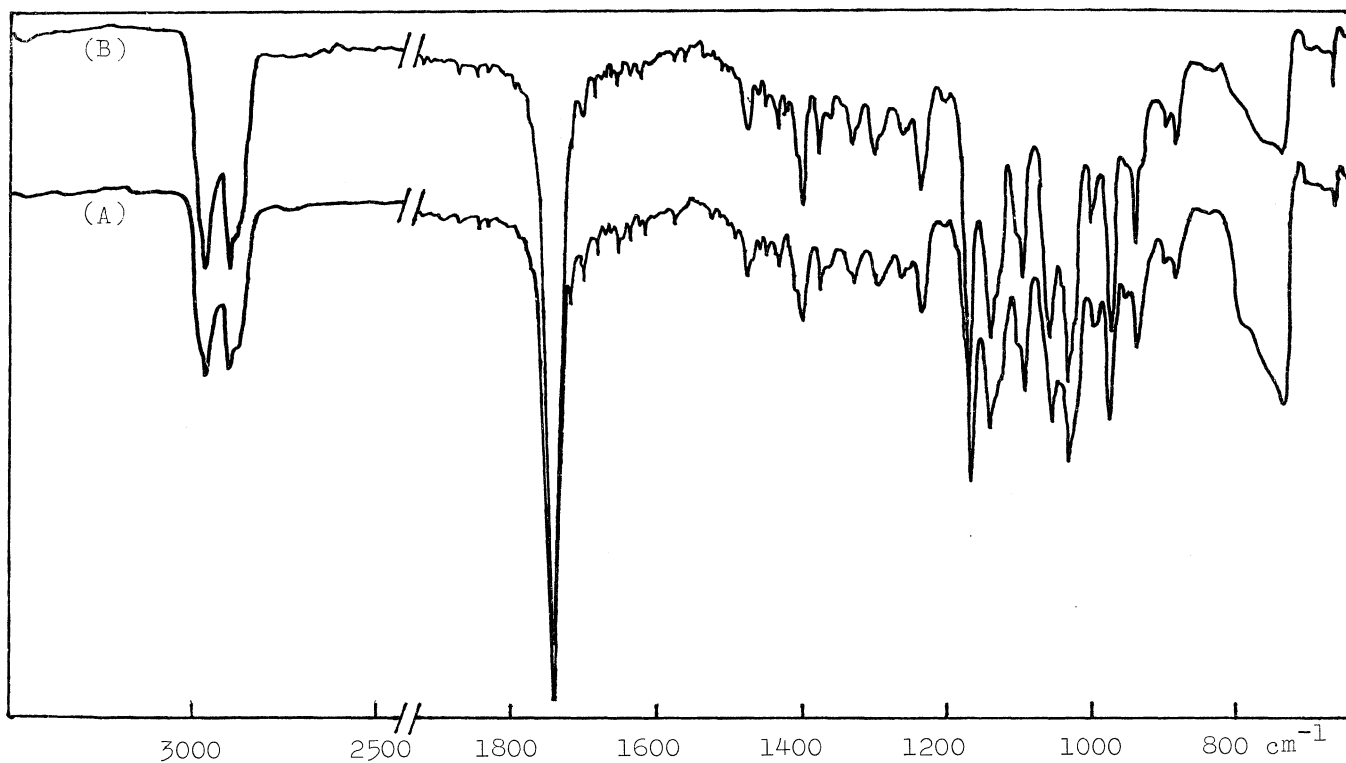


Fig. 1. Infrared spectra of DL-tetrahydroanhydroaucubigenone (A) and III (B). (in CCl<sub>4</sub>).

## References

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