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Santonin Analogs. IV. On an Isomeric Tetrahydroalantolactone obtained by the Reduction of Dihydroalantolactone.

A new procedure for obtaining both pure dihydroisoalantolactone (I) and dihydroalantolactone (II) in a good yield and an interesting observation during catalytic hydrogenation of (II) were reported in the 1st¹⁾ and 3rd²⁾ papers of this series. The present paper is concerned with the preparation of isomeric glycols, (VII) and (XIII), and isomeric lactones, (VI) and (XIV), by the same series of reaction on (I) and (II).

With the use of lithium aluminum hydride, (I) was reduced producing a compound (III), $C_{15}H_{26}O_2$, m.p. 129~131°, $[\alpha]^{26}_{D}$: +46.0°. (III) was converted to (I) again by a mild oxidation with dichromate. Therefore structure (III) is the logical reduction product.

The structure of (III) was further supported by the following reactions : A methyl hydroxycarboxylate (IV), $C_{16}H_{26}O_3$, m.p. 103~106°, which was obtained by the hydrolysis of (I) with sodium hydroxide and followed by methylation with diazomethane, was oxidized with dichromate to a methyl ketocarboxylate (V), $C_{16}H_{24}O_3$, $b.p_{0.05}$ 95~97°. (V) was reduced with lithium aluminum hydride to yield (III). The same series of reactions were tested for tetrahydroalantolactone (VI) and in this case also the corresponding glycol (VII), $C_{15}H_{28}O_2$, m.p. 111~113°, $[\alpha]^{23}_{D}$: −7.9°, methyl hydroxycarboxylate (VIII), $C_{16}H_{28}O_3$, m.p. 124~127°, and methyl ketocarboxylate (IX), $C_{16}H_{26}O_3$, $b.p_{0.05}$ 95° (2,4-dinitrophenylhydrazone, m.p. 118~120°), were obtained.

Since (VII) was obtained from (III) by catalytic reduction, the stereochemical configurations of these corresponding derivatives, except one double bond in the series of dihydroalantolactone, were found to be the same.

However, when these reactions were tested for dihydroalantolactone (II), the glycol, $C_{15}H_{26}O_2$, m.p. 78~81°, $[\alpha]^{23}_{D}$: +29.9°, the structure of which could be proposed as (X) because (X) was converted again to (II) by mild oxidation, was found to give a saturated glycol (XIII), $C_{15}H_{28}O_2$, m.p. 126~128°, $[\alpha]^{23}_{D}$: +23.9°, by catalytic reduction. This new saturated glycol was different from (VII) in its melting point and possessed an opposite optical rotation. On admixture of (XIII) and (VII), a marked depression of the melting point was observed. Thus, (XIII) is a stereochemically isomeric compound of (VII). The other reactions for (II) gave corresponding compounds as in the case of (I). Thus, (II) was converted into methyl hydroxycarboxylate (XI), $C_{16}H_{26}O_3$, m.p. 103~105°, and (XI) was further oxidized to give methyl ketocarboxylate (XII), $C_{16}H_{24}O_3$, $b.p_{0.08}$ 110~111° (2,4-dinitrophenylhydrazone, m.p. 188~190°).

Furthermore, the isomeric saturated glycol (XIII) was mildly oxidized with dichromate to give a lactone (XIV), $C_{15}H_{24}O_2$, m.p. 134~137°, $[\alpha]^{20}_{D}$: +37.9°, and this was reduced

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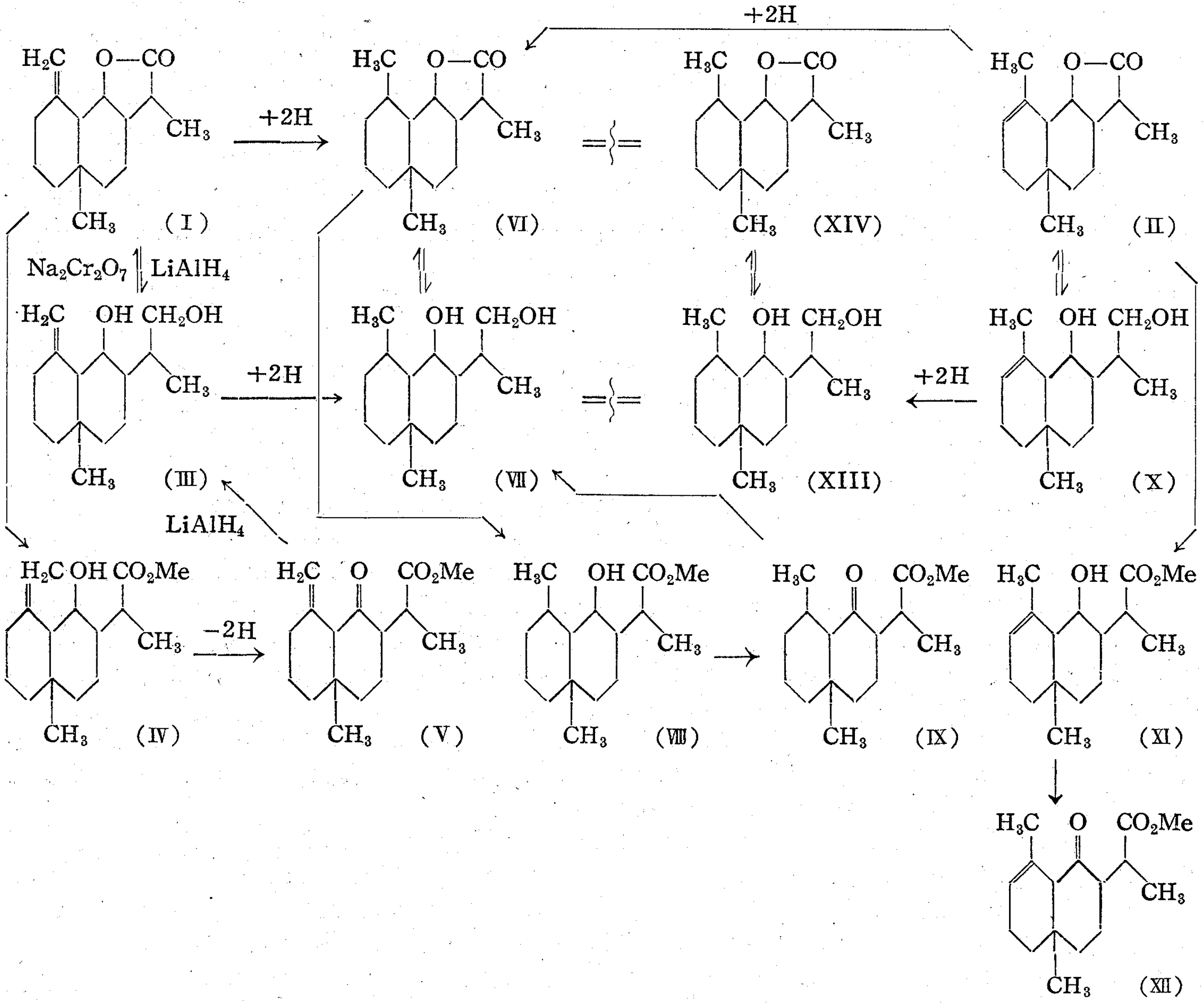
1) T. Ukita, R. Matsuda, S. Nakazawa : J. Pharm. Soc. Japan, **72**, 796 (1952).
2) T. Ukita, S. Nakazawa : This Bulletin, **2**, 239 (1954).

with lithium aluminum hydride to reproduce (XIII).

This lactone (XIV) was also found to have a different melting point and optical rotation from those of tetrahydroalantolactone (VI). (XIV) must also be a stereochemical isomer of (VI), and (XIV) will be referred to as "isotetrahydroalantolactone".

From the series of reactions mentioned above, a conclusion may be deduced that a migration of the double bond had occurred before the catalytic hydrogenation of (X). The reduction of the new double bond should then yield the isomeric saturated glycol (XIII). Research is being continued on the more exact mechanism of this interesting isomerization.

All compounds reported in this paper yielded satisfactory elemental analytical data.



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