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HYDROGENATIONS OF TRIACETIC ACID LACTONE. A NEW SYNTHESIS OF THE CARPENTER BEE (*Xylocopa hirsutissima*) SEX PHEROMONE

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Summary: under a variety of catalytic conditions, triacetic acid lactone, I, has been hydrogenated to differently oxidized lactones (II, III and V). C-Methylation of one of them, (II) is the key step for a convenient preparation of the carpenter bee sex pheromone.

Triacetic acid lactone is a natural polyketide lactone easily available by synthesis from the industrial dehydroacetic acid[1]. Its use as starting material for the preparation of more highly saturated natural lactones has not been studied. We present here our results concerning the hydrogenations of I under different catalytic conditions (Scheme 1).

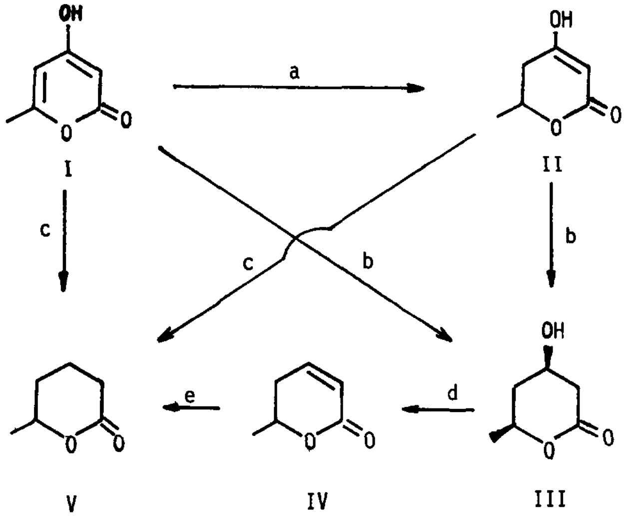
As previously described[2], hydrogenation (Pd/C) of I gave 4-hydroxy-6-methyl-5,6-dihydro-2-pyrone, II, m.p. 123-4°C. Hydrogenation of both I and II (Ra-Ni) led to the fully saturated and rather unstable alcohol *cis*-4-hydroxy-6-methyltetrahydro-2-pyrone[3], III, m.p. 41-3°C. The *trans*-isomer of III is a natural product present as a glycoside in *Sorbus aucuparia L*[4]. The *trans*-stereochemistry was well documented and rested upon the demonstration that the methyl group at C-6 was equatorial and that a value for $\Sigma J_{3,4}$ of 9Hz was found (H at C-4 equatorial, OH at C-4 axial). Our compound presented a $\Sigma J_{3,4}$ value of *ca*. 13Hz, compatible with H at C-4 being axial (OH equatorial), and therefore the *cis*-stereochemistry was attributed to III.

When both I and II were hydrogenated in the presence of a platinum catalyst, the fully reduced 6-methyltetrahydro-2-pyrone, V, was the only isolated compound. Its pmr spectrum was identical with that of an authentic specimen[5,12].

Dehydration of III to the known[6] 6-methyl-5,6-dihydro-2-pyrone (parasorbic acid), IV, was easily achieved by boiling in benzene in the presence of a catalytic amount of *p*-toluenesulphonic acid. We believe this synthesis compares well with others previously described[7,8]. As expected, hydrogenation of IV (Pd/C) led also to V.

One enantiomer of *cis*-3,6-dimethyltetrahydro-2-pyrone, IX, (see scheme 2), is the major volatile component of the carpenter bee sex pheromone[9]. Some syntheses have been described[9,10]. In particular, it is worth mentioning the work of Pirkle and Adams, which prepared the four possible stereoisomers (*cis* and *trans* in enantiomeric pure forms)[11,12], by separate methylation of

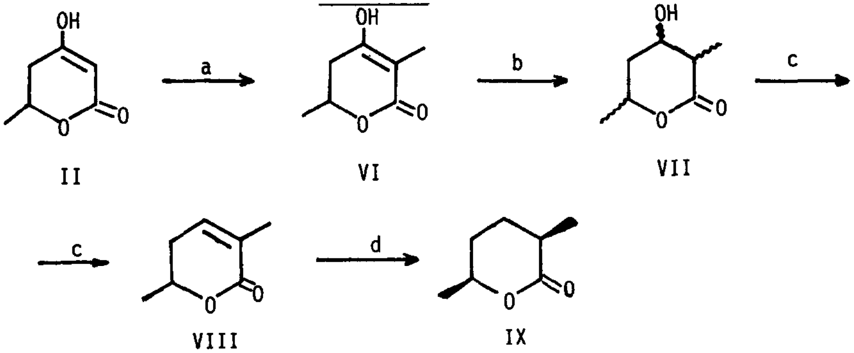
SCHEME 1



All compounds are racemic forms. Nearly quantitative yields were achieved in every step.

a: H_2, 1 atm., r.t. / 10 % Pd-C / EtOH
b: H_2, 1 atm., r.t. / Ni-Ra / EtOH
c: H_2, 1 atm., r.t. / Pt / AcOEt
d: TsOH / C_6H_6 / reflux
e: H_2, 1 atm., r.t. / 10% Pd-C / AcOEt

SCHEME 2



All compounds are racemic forms.
a: i-PrOLi / i-PrOH // ICH_3
b: H_2, 1 atm., r.t. / Pt / AcOEt
c: TsOH / C_6H_6 / reflux
d: H_2, 1 atm., r.t. / Pd-C / AcOEt

both enantiomers of V. However, all the described methods produce large amounts of the *trans* isomers XIV.

Our synthetic strategy required the methylation at the C-3 position at some step of the sequence. Investigations from this and other laboratories[13], have indicated that I can be O-methylated to X, but only minor amounts of the potential precursor XI are formed. However, after some experimentation, we have found that the partially hydrogenated II can be converted into 3,6-dimethyl-4-hydroxy-5,6-dihydro-2-pyrone[3,14], VI, m.p. 152-3°C, in 45% yield, under the conditions indicated in the scheme 2. Minor amounts of XII[3] and XIII[3] were also isolated from this reaction. The methylated lactone VI was hydrogenated under platinum catalysis to a mixture of alcohols VII, which without further purification was dehydrated to 3,6-dimethyl-5,6-dihydro-2-pyrone[3,14], VIII. Hydrogenation (Pd/C) of VIII from the less hindered side gave a mixture[14] of IX and XIV in a ratio of *ca.* 9:1. Separation of IX and XIV has been previously described[9,10,12]. The pmr spectrum of our 9:1 mixture was identical with that described for pure IX[9,12], and the elution order for both isomers in glc was also as described by the same authors. A cmr spectrum of a *ca.* 1:1 mixture of IX and XIV was available to us[10]. Our recorded spectrum was identical (but for the ratio of products), thus achieving further confirmation for the presence of XIV.

A full paper will be published including experimental details of this work and the synthesis of more natural lactones.

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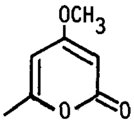
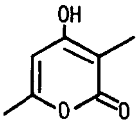
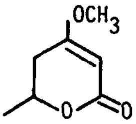


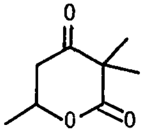
X



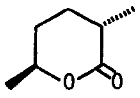
XI



XII



XIII



XIV

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14.- Correct elemental analysis was secured for this compound.

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