Syntheses in the Camphor Series. Alkylation of Quinones with Cycloalkyl Radicals. Attempted Syntheses of Lagopodin A and Desoxyhelicobasidin

J. GOLDMAN,* N. JACOBSEN and K. TORSSELL

Department of Organic Chemistry, University of Aarhus, DK-8000 Aarhus C, Denmark

In an attempt to synthesize lagopodin A and desoxyhelicobasidin, a new synthesis of (3R)-3-carboxy-3,4,4-trimethylyclopentanone and (1R)-1,2,2-trimethylyclopentanecarboxylic acid was worked out together with several other reactions in the camphor series. For the same purpose alkylation of quinones with cycloalkyl radicals derived from cycloalkane carboxylic acids by decarboxylation with silver ion sand peroxydisulphate was investigated and several cycloalkyl derivatives were prepared. It was not possible to add the sterically hindered trimethyl cyclopentyl radicals to quinones. The structure 22 is suggested for a camphor lactone claimed to be 21.

In previous papers we have described the alkylation of quinones with radicals from the decarboxylation of carboxylic acids with silver ions and peroxydisulphate (Eqns. 1 and 2)

\[
\begin{align*}
\text{Ag}^+ + \text{S}_2\text{O}_8^{2-} & \rightarrow \text{Ag}^+ + 2\text{SO}_4^{2-} \quad (1) \\
\text{Ag}^+ + \text{RCOOH} & \rightarrow \text{R} + \text{CO}_2 + \text{H}^+ + \text{Ag}^+ \quad (2)
\end{align*}
\]

In the present work the alkylation of quinones with cycloalkyl radicals was investigated in order to examine the possibility of synthesizing the naturally occurring terpenoid quinones lagopodin A and desoxyhelicobasidin 2 by this method.

During the search for a convenient synthesis of the carboxylic acids 3 and 4, required for this purpose, some other useful reactions in the camphor series were discovered. These are discussed in the section containing the syntheses of 3 and 4.

RESULTS

Alkylation of 1,4-naphthoquinones 5. The alkylation of 1,4-naphthoquinone 5 and 2-methyl-1,4-naphthoquinone 6 with cycloalkyl radicals \((\text{C}_9 - \text{C}_4)\) gave the corresponding cycloalkylquinones in fair yields (Table 1).

The possibility of generating cyclopentyl radicals indirectly by the cyclisation of an open chain unsaturated radical (Eqn. 3) was also examined.

\[
\begin{align*}
\text{COOH} & \rightarrow \text{COOH} + \text{H}^+ \quad (3)
\end{align*}
\]

When 5-hexenoic acid was decarboxylated in the presence of 2-methyl-1,4-naphthoquinone, 2-methyl-3-(4-pentenyl)-1,4-naphthoquinone 12 was isolated. Only traces of the cyclopentylquinone 9 could be detected.

Table 1. Alkylation of quinones with cycloalkyl radicals.

<table>
<thead>
<tr>
<th>Quinone</th>
<th>Carboxylic acid</th>
<th>Product</th>
<th>Yield %</th>
<th>m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Cyclopropane-7</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>37</td>
<td>82-83°</td>
</tr>
<tr>
<td>6</td>
<td>Cyclobutane-8</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>56</td>
<td>59-60°</td>
</tr>
<tr>
<td>6</td>
<td>Cyclopentane-9</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>42</td>
<td>96-97°</td>
</tr>
<tr>
<td>6</td>
<td>Cyclohexane-10</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>45</td>
<td>78-79°</td>
</tr>
<tr>
<td>5</td>
<td>Cyclohexane-11</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>55</td>
<td>87-88° (lit.5 87-88)</td>
</tr>
</tbody>
</table>

*Synthesis of 3 and 4.* Since the published syntheses of the optically active or the racemic 3 are rather complicated, a new route to 3 and 4 in their optically active forms was investigated.

Oxidative decarboxylation of (1R)-cis-camphoric acid-1-methylester 13 with lead tetraacetate in the presence of cupric ions by the method of Kochi gave (1R)-1,2,2-trimethylcyclopent-3-ene-carboxylic acid methylester 14.

Alkaline hydrolysis of 14 gave the corresponding carboxylic acid 15 which was hydrogenated catalytically to 4 (1R-configuration).

The oxidative decarboxylation of 13 was also performed by the use of silver ion-peroxydisulphate-cupric ions in water-acetonitrile in the same yield but with higher conversion of 13. In this reaction the presence of pyridine proved essential for the oxidation of the intermediate radical 16 to 14 by the cupric ions. When the reaction was carried out in the absence of pyridine, a mixture of 14 and the saturated ester 17 (Scheme 1) was formed.

To investigate the selectivity of the oxidative decarboxylation between secondary and tertiary carboxyl groups with both lead tetraacetate and silver ion-peroxydisulphate, camphoric acid was decarboxylated by both oxidants under conditions similar to those in the syntheses of 14.

Two radicals, 18 and 19, result from the decarboxylation of the secondary and the tertiary carboxylic group, respectively.

Scheme 1.

The main products in both reactions were the lactones 20 and 21 formed from 18 and 19, respectively, probably by internal ligand-transfer, and analogously 19→21.

The expected products, cyclopentenoic acids (formed analogously to 14) were only present in small amounts.

These results show that the tertiary carboxylic group is decarboxylated much faster than the secondary by both reagents.

The spectra and physical data of 21 were very different from those published by Hayashi et al. for a compound claimed to be 21. Their data are in better agreement with the structure 22, also considered by these authors. A comparison of the two sets of data is given in Table 3.

Table 2. Ratio* of products from decarboxylation of camphoric acid.

<table>
<thead>
<tr>
<th>Oxidant</th>
<th>20 (%)</th>
<th>21 (%)</th>
<th>total yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pb(OAc)$_4$</td>
<td>17</td>
<td>83</td>
<td>64</td>
</tr>
<tr>
<td>Ag$^{+}$/S$_2$O$_5$$^{2-}$</td>
<td>5</td>
<td>95</td>
<td>57</td>
</tr>
</tbody>
</table>

* Determined by GLC.

Attempts to bring about the conversion 15→23 by hydroboration of 15 or its tetrabutyl-
Table 3. Comparison of the physical data of 21 and 22.

<table>
<thead>
<tr>
<th></th>
<th>Compound 21</th>
<th>Compound of Hayashi et al.* 22</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IR</strong></td>
<td>1775 cm⁻¹ (5-membered lactone), supports 21</td>
<td>1730 cm⁻¹ (6-membered lactone), supports 22</td>
</tr>
<tr>
<td><strong>NMR</strong></td>
<td>see Experimental, supports 21</td>
<td>integral of methyl signals: other</td>
</tr>
<tr>
<td></td>
<td></td>
<td>protons = 9:7, supports 22</td>
</tr>
<tr>
<td><strong>MS</strong></td>
<td>no peaks beyond 154 (M⁺ for 21). Fragmentation pattern very</td>
<td>peak at 168 (M⁺ for 22). Fragmentation</td>
</tr>
<tr>
<td></td>
<td>similar to 20, supports 21</td>
<td>pattern very different from that of 20, supports 22</td>
</tr>
<tr>
<td><strong>Analysis</strong></td>
<td>see Experimental, supports 21</td>
<td>supports both 21 and 22</td>
</tr>
<tr>
<td><strong>M.p.</strong></td>
<td>113 – 115 °C</td>
<td>156 – 157 °C</td>
</tr>
</tbody>
</table>

\[ \begin{align*}
\text{15} & \overset{\text{Br}_2}{\rightarrow} \text{16} \\
\text{24} & \overset{\text{OH}^-}{\rightarrow} \text{25} \\
\text{25} & \overset{\text{H}_2/\text{Pd-C} \text{MgO}}{\rightarrow} \text{20}
\end{align*} \]

Scheme 2.

ammonium salt with disiamylborane, followed by oxidation with hydrogen peroxide by the method of Brown,* were unsuccessful.

Bromination of 15 gave a dibromoderivative 24 which, when treated in situ with aqueous sodium carbonate, gave a bromolactone 25. Catalytic hydrogenation of 25 gave 20 which on hydrolysis and oxidation would lead to an isomer of the desired keto acid 3.

The endo-configuration of 25 was deduced as follows: The carboxylate ion in the dibromacid 24 substitutes the bromine atom in trans position, and since the addition of bromine to the double bond proceeds in a trans fashion, the bromine of 25 is located cis to the lactone bridge (Scheme 2).

Treatment of 15 with p-toluene sulphonic acid in refluxing toluene gave the desired lactone 26, together with a minor amount (13 %) of 20. It proved impossible to separate 20 from 26 by other means than preparative GLC so the mixture was hydrolyzed and the (1R)-cis-4-hydroxy-1,2,3-trimethylcyclopentanecarboxylic acid 23 was purified by crystallization from water.

Oxidation of 23 by chromic acid in a 2-phase system gave 3 in good yield.

*Attempted syntheses of lagopodin A and desoxyhelicobasidin 2. As a model of the synthesis of desoxyhelicobasidin we used naphthoquinone with 4 but without success, partly because of the low solubility of 4 in water and aqueous acetonitrile which caused formation of a 2-phase system on addition of peroxydisulphate
and thereby ineffective decarboxylation of A. The same reaction using A as its silver- or tetrabutylammonium salt or A together with a weak base like 2,6-lutidine, gave no alkylated naphthoquinone, although A was consumed in these reactions.

To overcome the solubility problem, we tried to carry out the alkylation with 15 instead of A but in this reaction the simple alkylated naphthoquinone 27 was not obtained.

Instead 28 was formed as the only isolable quinone product in a yield of 41% (apparently only the endo-isomer).

The endo structure was preferred for the following reason: The NMR coupling constants, of the $H_A$, $H_B$, and $H_X$ protons, of 28 are in reasonably good agreement (Table 4) with those of the bromola lactone 25 which for reasons already mentioned should be the endo-isomer.

We are not, however, able to find sufficient NMR data of related structures in the literature to justify a definite assignment.

Two mechanisms, 5A and 5B, for the formation of 28 can be formulated, see below.

In view of the small gain in energy by cyclization of 29 compared with the greater amount of energy liberated by a decarboxylation, 30 is preferred to 29 as intermediate.

The mechanism B has also been proposed by Moriarty 18 for the oxidation of various alkenecarboxylic acids by lead tetraacetate.

Attempts to alkylate toluquinone with 3 to give lagopodin A and isomers also failed, indicating that the steric hindrance of the tertiary cycloalkyl radicals in the alkylation step is of such a magnitude that the fast oxidation of these radicals by Ag$^{+}$ or SO$_4$$^-$$^-$ prevails.

In agreement with this alkylation with 1-methylocyclohexanecarboxylic acid also gave very poor yields.

**EXPERIMENTAL**

Melting points are uncorrected. NMR spectra were recorded on a Varian A-60, IR spectra on a Perkin-Elmer Infracord, and UV spectra on a Perkin-Elmer 402 spectrometer. Analytical GLC was performed with a Perkin-Elmer F11 chromatograph. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. Calculation of NMR shifts and coupling constants was made by means of the LAOCN-3 programme.

Alkylation of quinones. Details of the reaction have been described earlier.1

**General procedure.** To a vigorously stirred water-acetonitrile solution of the quinone, the

<table>
<thead>
<tr>
<th>Compounds</th>
<th>$J_{AB}$</th>
<th>$J_{AX}$</th>
<th>$J_{BX}$</th>
<th>$J_{XY}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>-15.2</td>
<td>10.1</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>28</td>
<td>-13.9</td>
<td>10.7</td>
<td>5.1</td>
<td>1.7</td>
</tr>
</tbody>
</table>

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carboxylic acid, and silver nitrate at 60 - 65 °C an aqeous solution of ammonium peroxysodium
 sulphate was added during 45 min. After a further 10 min stirring at 60 - 65 °C, the mixture
 was cooled to room temperature and extracted with ether. The ether phase was washed with
 aqueous NaHCO₃ until neutral, dried, and evaporated. The crude products were chromatographed,
 either on TLC plates (silica gel Merck); procedure A: eluent 20 % ether in petrol ether;
 procedure B: eluent CH₂Cl₂ or on a column of neutral alumina; procedure C: eluent CH₂Cl₂.

2-Cyclopropyl-3-methyl-1,4-naphthoquinone, 7.
To 2-methyl-1,4-naphthoquinone (1.72 g, 0.01 mol), cyclopropane-carboxylic acid (1.29 g, 0.015 mol),
and silver nitrate, 0.5 g, in acetonitrile (25 ml) and water (60 ml) was added ammonium
peroxysulphate (3.42 g, 0.015 mol) in water (20 ml). Chromatography (procedure A) gave
10, 1.16 g (46 % calculated on the quinone), m.p. 78 - 79 °C. (Found: C 80.0; H 7.24. Calc.
for C₇₅H₅₂O₅: C 80.3; H 7.15). UV (EtOH): λ_max nm (log e) 246 (4.28), 250, sh, 289, sh,
275 (4.11), 331 (3.5). IR (CCL₄): 1660(s), 1585(m). NMR (CCL₄): δ 1.0 - 2.2 (10 H, m), 2.17 (3 H,
s), 2.4 - 3.1 (1 H, m), 7.5 - 8.1 (4 H, m).

2-Cyclohexyl-1,4-naphthoquinone, 11. To 1,4-
naphthoquinone (1.58 g, 0.01 mol), cyclohexane-
carboxylic acid (1.92 g, 0.015 mol), and silver nitrate (0.5 g) in acetonitrile (22 ml) and water
(20 ml) was added ammonium peroxysulphate (3.42 g, 0.015 mol) in water (15 ml). Chromatography
(procedure A) of the crude product gave II, 1.32 g (55 % based on the quinone), m.p.
87 - 88 °C (lit. 87 - 88 °C). UV (EtOH): λ_max nm (log e) 248 (4.26), 255 (4.24), 267 (4.17), 334
(3.5). IR (CCL₄): cm⁻¹ 1665(s), 1585(m), 1595(m). NMR (CCL₄): δ 0.9 - 2.4 (10 H, m), 2.4 - 3.2 (1 
H, m), 6.61 (1 H, d, J = 7), 7.5 - 8.2 (4 H, m).

3-Methyl-2-(4-pentenyl)-1,4-naphthoquinone, 12. To 1-methyl-1,4-naphthoquinone (1.72 g, 0.01 mol),
5-hexenoic acid (1.71 g, 0.016 mol), and silver nitrate (0.5 g) in acetonitrile (25 ml) and water
(25 ml) was added ammonium peroxysulphate (3.42 g, 0.015 mol) in water (15 ml). Chromatography
(procedure B) of the crude product gave 12, 920 mg (38 % based on the quinone), m.p. 46 - 47 °C. (Found: C 79.6; H 6.75. Calc. for C₁₆H₁₂O₂: C 80.0; H 6.71). UV (EtOH): λ_max nm (log e) 249 (4.19), 267 (4.15),
273 (4.15), 333 (3.4). IR (CCL₄): cm⁻¹ 1660(s), 1620(m), 1595(m). NMR (CCL₄): δ ~ 1.5 (2 H, distorted 
quintet, J = 7), 2.1 (2 H, b, t, J = 7), 2.10 (3 H, s), 2.5 (2 H, d, t, J = 8, J' = 7), 4.8 - 5.3 (2 H, m),
5.6 - 6.2 (1 H, m), 7.5 - 8.1 (4 H, m). Only traces of 9 could be detected by TLC.

2-(endo-5)-1,7,7-Trimethyl-2-oxo-3-oxa-bicyclo[2.2.1]heptyl-1,4-naphthoquinone, 25. To
1,4-naphthoquinone (0.79 g, 0.005 mol), 15 (0.93 
g, 0.006 mol), and silver nitrate (0.5 g) in acetonitrile (15 ml) and water (20 ml) was added ammonium
peroxysulphate (1.30 g, 0.0057 mol) in water (8 ml). Chromatography (procedure C) gave 25, 940 mg (41 % calculated on the
quinone), m.p. 132 - 133 °C (after recrystallization
from methanol and from cyclohexane).

[x]₂₅° = -158° (ethanol, e = 0.5) (Found: C 72.9; 
H 5.79. Calc. for C₁₆H₁₂O₂: C 73.5; H 5.84). UV (EtOH): λ_max nm (log e) 248 (4.21), 254
(4.21), 264 (4.09), 339 (3.4). IR (CCL₄): cm⁻¹ 1755(s), 1655(s), 1625(m), 1600(m). NMR
(CDC₁₉): δ 1.0 (3 H, s), 1.15 (3 H, s), 1.17 (3 H, s), 1.71* (1 H, A part of ABXZY system),
2.32* (1 H, B part), 3.84* (1 H, X part), 4.80
(1 H, d, Y part, JXY = 1.7), 6.82 (1 H, d, Z part, 
JZX = 1.5), 7.6 - 8.3 (4 H, m). JAX* = -13.9, 
JAX* = 10.7, JBX* = 5.1. The signal at δ 3.84,
which appeared as four triplets, was changed

* Calculated values.
into four doublets, $J = 1.7$, by irradiation of the doublet at 6.82.

**Dimethyl-(IR)-cis-camphorate** was prepared by the method of Riedel 11 in a yield of 97%. NMR (CCl₄): 0.72 (3 H, s), 1.18 (3 H, s), 1.21 (3 H, s), 1.3 - 2.9 (5 H, m), 3.65 (6 H, s).

**(-IR)-Camphoric acid-1-methylester**, 13. 123 g (0.54 mol) of dimethyl-(IR)-cis-camphorate and potassium hydroxide (0.54 mol) were dissolved in methanol (800 ml) and water (400 ml) and left at room temperature for 3 days. The solution was refluxed for 30 min with the methanol was distilled off. The aqueous phase was washed with ether, acidified with conc. HCl and extracted with CH₂Cl₂. Drying and evaporation of the CH₂Cl₂ phase gave 108 g (94%) of almost pure 13, m.p. 85 - 86 °C (from petrol ether) (lit. 12 80 - 87 °C) (2, pyridine (11 g) in benzene (450 ml) was refluxed with stirring for 2 h. The reaction mixture was filtered, washed with dilute nitric acid to remove pyridine and copper salts and extracted with aqueous potassium carbonate until neutral. On acidification of the alkaline washings, 13 g of 13 were recovered. The benzene phase was dried and distilled. The fraction boiling at 180 - 186 °C was (12)-1,2,2-trimethycyclopetan-3-ene-1-carboxylic acid methylster, 14, 19.5 g (73% based on converted 13). (For use in the hydrolysis it is only necessary to distill off the benzene). N₂H₄ = 1.4501, (2) = 113° (ethanol, c=1). IR (CCl₄): cm⁻¹ 1735(s), 1620(w). NMR (CCl₄): δ 0.88 (3 H, s), 1.13 (3 H, s), 1.18 (3 H, s), 2.0 (1 H, distorted d, J = 17), 3.2 (1 H, distorted d, J = 17), 3.66 (3 H, s), 5.3 (1 H, m), 5.5 (1 H, m).

**Decarboxylation of 13 with Ag⁺/S₂O₄²⁻**. To a stirred mixture of 13 (21.4 g, 0.1 mol) cupric sulphate (8 g), silver sulphate (4 g), and pyridine (6 ml) in water (150 ml) and acetonitrile (100 ml) at 60 - 70 °C was added ammonium peroxodisulphate (30.6 g, 0.13 mol) in water (50 ml) during 1 h while the pH was kept at 6 - 7 by addition of 4 M sodium hydroxide. After a further 10 min stirring, 4 M sulphuric acid (100 ml) was added and the mixture was cooled and extracted three times with petrol ether. The organic phase was dried and the petrol ether was distilled off together with some acetonitrile leaving almost pure 14 (11.8 g, 70%) containing less than 1% of 17 (GLC, 5% SE-30, using authentic samples as references). In the absence of pyridine it was necessary to use more acetonitrile (140 ml) and less water (90 ml) to bring 13 in solution, and the crude product was very impure and had to be distilled before GLC analysis. The fraction, boiling at 106 - 130 °C/45 mm, (7.8 g, 46%) was collected and found to contain 14 (71%) and 17 (29%) by GLC.

1,2,2-Trimethycyclopetan-3-ene-1-carboxylic acid, 15. A solution of 14 (7.7 g, 0.046 mol) and potassium hydroxide (35 g, 0.63 mol) in methanol (170 ml) and water (15 ml) was refluxed for 20 h. The methanol was distilled off, the residue was dissolved in water and washed with ether. The aqueous phase was cooled to 0 °C, acidified with conc. HCl, and the precipitated (IR)-1,2,2-trimethycyclopetan-3-ene-1-carboxylic acid 15 filtered, washed with cold water, and dried. Yield: 5.9 g (84%), m.p. 157 - 158 °C (from formic acid or aqueous formamide or after sublimation at 120 °C/10 mm, lit. 12 157 - 159.5 °C). [α]D²⁰ = +123° (ethanol, c=1). IR (CHCl₃): cm⁻¹ 2500 - 3500, 1705(s), 1625(w). NMR (CCl₄): δ 1.02 (3 H, s), 1.17 (3 H, s), 1.27 (3 H, s), 2.0 (1 H, distorted d, J = 17), 3.2 (1 H, distorted d, J = 17), 3.5 (1 H, m), 5.5 (1 H, m), 11.9 (1 H, s).

**Decarboxylation of (IR)-cis-camphoric acid** by lead tetracetate. Preparation of 19 and 21. Camphoric acid (10 g, 0.05 mol), lead tetracetate (27.8 g, 90% pure, 0.055 mol), neutral cupric acetate (2 g), and pyridine (3 ml) were refluxed in benzene (200 ml) for 3 h. The mixture was washed with 30% nitric acid, water, and aqueous sodium carbonate, successively, dried, and evaporated in vacuo at room temperature leaving 4.9 g (64%) of a mixture of 20, 17% and 21, 83% (GLC). On acidification of the sodium carbonate phase, ca. 1.5 g of acidic material — mainly camphoric acid — was obtained.

**Decarboxylation of (IR)-cis-camphoric acid with Ag⁺/persulphate.** Camphoric acid (10 g, 0.05 mol), cupric sulphate (2 g), silver sulphate (2 g), pyridine (3 ml), water (200 ml), and acetonitrile (20 ml) were stirred at 60 - 65 °C while 13.68 g (0.06 mol) of ammonium peroxodisulphate in water (50 ml) were added during 70 min. During the addition, the pH was kept at 5 - 7 by addition of diluted NaOH. After a further 10 min stirring at 60°C, 2 M H₂SO₄ (50 ml) was added and the mixture was extracted with ether. The ether extract was washed with aqueous sodium carbonate, dried, and evaporated to give 4.4 g (57%) of a mixture of 20 and 21 (5.95, GLC). Small amounts of acidic material could be obtained on acidification of the carbonate phase. Preparative GLC 10% PEG of the mixture gave 21, m.p. 113 - 115°C [α]D²⁰ = +12.6° (ethanol, c=0.5). (Found: C 70.0; H 8.10. Calc. for C₂₀H₂₂O₂: C 70.1; H 8.15.) IR (KBr): cm⁻¹ 1775(s). NMR (CCl₄): δ 0.95 (3 H, s), 1.06 (3 H, s), 1.39 (3 H, s), 1.5 - 2.1 (4 H, m), 2.28 (1 H, distorted dd). MS Mass % of base peak): 154 (5) M⁺, 139 (5), 126 (31), 111 (27), 108 (28), 95 (100).

**Lactonisation of 1,2,2-trimethycyclopetan-3-ene-carboxylic acid, 15.** Preparation of 20 and 20. 15 (5.85 g, 0.056 mol) and p-toluene sulphonic acid (4.3 g, 0.027 mol) were refluxed for 20 h in

toluene (70 ml). The mixture was extracted with aqueous sodium carbonate. On acidification of the carbonate washing, 15 (1.35 g) was recovered by extraction with CH₂Cl₂. The toluene phase was dried and evaporated in vacuo at room temperature. The residue was sublimated at 115 °C/10 mm to give 4.08 g (57%) of a mixture of (1R)-cis-4-hydroxy-1,2,2-trimethylcyclopentanecarboxylic acid lactone, 26, and the isomeric 3-hydroxy cycroxylic acid lactone, 20, ratio 87:13 (GLC, 10% PEQ). This mixture could not be separated by crystallization. The IR spectrum of the mixture was almost identical with the spectrum of 26, published by Faigle and Karrer. NMR (CCl₄) of 26: After subtraction of the signals from 20 \( \delta \) 0.97 (3 H, s), 1.07 (3 H, s), 1.10 (3 H, s), 1.7 (2 H, m), 1.9 (2 H, m), 4.6 (1 H, m).

(1R)-cis-4-Hydroxy-1,2,2-trimethylcyclopentanecarboxylic acid, 23. The lactone mixture of 20 and 26 (4 g) was refluxed for 20 h with 40 g KOH in 160 ml of methanol and 80 ml of water. The methanol was evaporated and the aqueous phase washed with ether, acidified with conc. HCl and extracted with several portions of CH₂Cl₂. The CH₂Cl₂ phase was dried and evaporated and the residue recrystallized from water giving pure 23 (2.95 g, 66%), m.p. 190 – 200 °C (lit. 200 °C). \([\alpha]_D^{20} = +14°\) (ethanol, c = 4).

IR (KBr): cm⁻¹ 3400(s), 2500 – 3100(s), 1700(s). NMR (D₂O, K₂CO₃): \( \delta \) 0.93 (3 H, s), 0.98 (3 H, s), 1.01 (3 H, s), 1.38 – 2.37 (4 H, m), 4.07 – 4.50 (1 H, m).

(1R)-3-Carboxy-3,4,4-trimethylcyclopentanone, 3. To 23 (1.087 mol) dissolved in 20 ml of water and dimethylether (3.5 ml) was added at 25°C in a solution of Na₂Cr₂O₇.2H₂O (1.6 g, 0.054 mol) and conc. H₂SO₄ (1 g) in water (15 ml) with vigorous stirring during 15 min. After further 4 h of stirring, the organic layer was separated and the aqueous phase extracted several times with ether. The combined organic phases were dried and evaporated to give 3 (1.20 g, 81%), m.p. 220 – 221°C (from H₂O (lit. 221°C)). \([\alpha]_D^{20} = +23°\) (ethanol, c = 2). IR (CCl₄): cm⁻¹ 2500 – 3300(s), 1745(s), 1700(s). NMR (CDCl₃): \( \delta \) 1.14 (3 H, s), 1.21 (3 H, s), 1.35 (3 H, s), 2.20 and 3.01 (2 H, AB system, \( J_{AB} = 19° \), 2.36 (1H, b, s), ~11 (1 H, b, s).

(1R,1S,2,2,2-Trimethylcyclopentanecarboxylic acid, 4. 15 (10.0 g, 0.065 mol) in 100 ml alcohol was hydrolyzed over 5 % Pd/C (0.6 g) for 20 h at room temperature and 1 atm. The solution was filtered and evaporated and the residue recrystallized from acetonitrile to give 4 (5.3 g, 82%), m.p. 191 – 192 °C (lit. 192 – 193 °C). \([\alpha]_D^{20} = +20°\) (ethanol, c = 1). IR (CCl₄): cm⁻¹ 2500 – 3300(s), 1700(s). NMR (CDCl₃): \( \delta \) 0.98 (3 H, s), 1.07 (3 H, s), 1.18 (3 H, s), ~1.6 (5 H, m), 2.0 – 2.7 (1 H, m), 11.77 (1 H, s).

Methyl-(1R,1S,2,2,2-trimethylcyclopentanecarboxylate, 17. To 4 (4.68 g, 0.03 mol) and sodium hydride (1.6 g, 0.039 mol) in 20 ml of water at 40°C was added dimethyl sulphate (3.4 ml, ~0.036 mol). The temperature was kept at 60°C for 1 h and excess of NaOH was added. The product 17 was extracted with ether and distilled (3.6 g, 71%), b.p. 176 – 180 °C. \( n_\text{D}^{20} = 1.4448. [\alpha]_D^{20} = +8.4°\) (ethanol, c = 3). IR (film): cm⁻¹ 1740(s). NMR (CCl₄): \( \delta \) 0.81 (3 H, s), 1.01 (3 H, s), 1.10 (3 H, s), 1.6 (5 H, m), 2.0 – 2.7 (1 H, m), 3.89 (3 H, s).

(1R,2S)-3-Bromo-cis-4-hydroxy-1,2,2-trimethylcyclopentanecarboxylic acid lactone, 25. To 15 (10.0 g, 0.065 mol) in chloroform (30 ml) kept below 5°C was added bromine (11.5 ml, 0.072 mol) during 1 h. After the addition, the mixture was stirred at 5°C for 30 min. The CHCl₃ was evaporated and the residue was vigorously with 10 % Na₂CO₃ (120 ml) for 1 h. Extraction of the mixture with methylene chloride, drying, and evaporation gave 13.8 g of a crystalline product which was recrystallized from petrol ether (b.p. 60 °C) to give pure bromolactone 25 (11.9 g, 72%), m.p. 90.5 – 91.5°C. (Found: C 46.5; H 5.75; Br 34.2. Calc. for C₁₉H₁₄O₂Br: C 46.4; H 5.62; Br 34.3). \([\alpha]_D^{20} = -71°\) (ethanol, c = 1). IR (CCl₄): cm⁻¹ 1785(s), NMR (CCl₄): \( \delta \) 1.01 (3 H, s), 1.04 (3 H, s), 1.09 (3 H, s), 1.82 (1 H, A part of ABXY system), 2.60 (1 H, B part), 4.26 (1 H, X part), 4.53 (4 H, Y part), \( J_{AB} = 15.2°, J_{AX} = 4.0°, J_{BX} = 10.1°, J_{XY} = 2.0°\).

Catalytic hydrogenation of bromolactone, 25. 25 (2.34 g, 0.01 mol) in methanol (20 ml) was hydrogenated over 1 g of 5 % Pd/C and 4 g of MgO (1 atm, 25°C) until slightly more than 0.01 mol of hydrogen was consumed (28 h). The solution was filtered, diluted with water (100 ml) and extracted 5 times with methylene chloride. The organic phase was washed with aqueous K₂CO₃, dried, and evaporated and the residue sublimated at 100°C/10 mm to give 20, 910 mg (59%), m.p. (from ether) 162 – 164°C (lit. 165 – 167°C). The IR spectrum was identical with that published by Faigle and Karrer, \( [\alpha]_D^{20} = -19°\) (ethanol, c = 2). NMR (CCl₄): \( \delta \) 0.92 (3 H, s), 0.98 (3 H, s), 1.01 (3 H, s), 1.4 – 2.1 (4 H, m), 4.23 (1 H, m). MS: Mass (intensity – % of base peak): 154 (2) M⁺, 140 (2), 126 (10), 111 (10), 106 (18), 97 (18), 86 (100).

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