Pergamon

Tetrahedron Letters, Vol. 37, No. 27, pp. 4705-4706, 1996

0040-4039/96 \$15.00 + 0.00

PII: S0040-4039(96)00911-2

Oxidative Degradation of Larixol and Larixyl Acetate.

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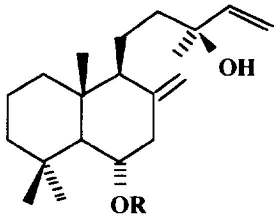
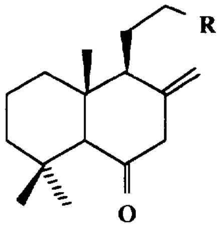
Abstract: A side-chain selective cleavage of larixyl acetate and larixol is presented.

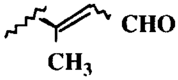
Larixol **1** and in particular its 6-acetate (larixyl acetate) **2** are major constituents (> 10 %) of the oleoresins of several *Larix* species, such as *L. decidua*, *L. gmelini*, *L. eurolepsis* and *L. pendula* .[1-3] Several degradative studies of larixol have been carried out but they do not appear to be of preparative value.[4-10] Very recently, however, larixol has been suggested[11] as starting material for the synthesis of various diterpenes, which prompts us to disclose at this time our related results.

To preserve existing ring functionality a selective degradation of the side-chain was required. Larixol was at first oxidized with potassium dichromate to afford, beside a minor amount (*ca.* 10 %) of larixone,[12] a mixture of conjugated aldehydes **3** (60 %). These were not separated, but further oxidized (CrO_3 / AcOH) to provide diketone **4** (30 %). The overall yield of **4** could be substantially improved (50 %) by treating **1** directly with chromium trioxide in acetic acid. It is of interest to note that under those conditions, isomerisation of **4** to the conjugated enone [9,11] is not observed. While the transformation **1** to **4** was relatively efficient, the presence in **4** of two keto groups complicated subsequent modification and led us to oxidize instead larixyl acetate.



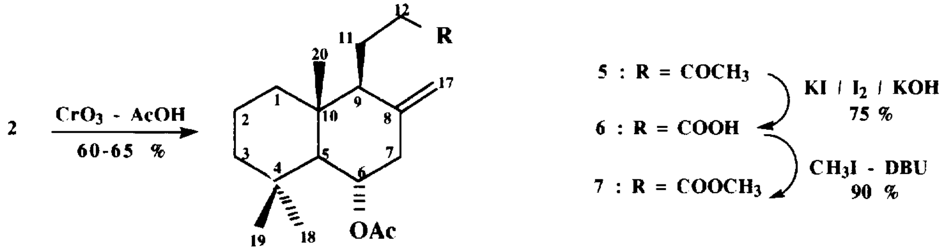
1 : **R** = **H**
2 : **R** = **Ac**



3 : **R** = 

4 : **R** = **COCH$_3$**

Readily available [1-3] larixyl acetate **2**, upon treatment with potassium permanganate, gave a monoketone, **5** [13], but isolated yields were low (*ca.* 30 %), presumably due to the extraction difficulties encountered. Chromium trioxide, however, was effective in the oxidation of **2** and **5** could thus be obtained on a multi-gram scale in over 60 % yield. In contrast to **4**, ketoacetate **5** offers the advantage of having three different functionalities and thus becomes a valuable building block for selective further transformation.[14] For example, oxidation of the keto group of **5** could be carried out through a Lieben iodoform reaction [15] to give carboxylic acid **6**[13] in good yield ; esterification of **6** (diazomethane (quant.) or DBU, methyl iodide[16]) then provided **7**.[13] With a route to building blocks **4-7** in hand, we are continuing our work toward the synthesis of labdanoids.[17]



Acknowledgements: F. Cottin (Office National des Forêts, Secteur de Briançon, France) is warmly thanked for collecting the oleoresin of *Larix decidua* (French Alps, summer of 1995). The translation of Russian literature by A. Alimardanov (Case Western Reserve University, Cleveland,USA) is gratefully acknowledged.

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13. For the sake of clarity, larixol numbering has been kept. **5**: $[\alpha]_D^{23}$ = + 51 (c=1, $CHCl_3$). IR : 1740 (OCO-CH_3) 1715 (CO);^{1}H-nmr (300 MHz-$CDCl_3$): 5.0 (dt, J =11 and 5, 1H, H-6), 4.9 and 4.5 (2 s, 2H, H-17 and H-17'); 2.65 (dd, J =12 and 5, 1H, H-7β); 2.1 (s, 3H, $COCH_3$); other CH_3's at 1.00, 0.85 and 0.70. ^{13}C-nmr (50 MHz-$CDCl_3$): 208.9 (C-13), 169.9 ($OCOCH_3$),143.9 (C-8), 109.2 (C-17), 73.0 (C-6), 57.3 (C-5), 55.1 (C-9), 44.0, 43.3, 42.5, (C-3, C-7, C-12), 39.6 (C-10), 38.9 (C-1), 36.0 (C-18), 33.4 (C-4), 29.9 ($COCH_3$),22.3 (C-19), 21.8 ($OCOCH_3$), 18.9 and 17.5 (C-2 and C-11), 15.7 (C-20). **6** : $[\alpha]_D^{23}$ =+ 49 (c=0.4, $CHCl_3$). IR : 1715 (COOH);^{1}H-nmr (200 MHz-$CDCl_3$): 10.2 (b s, COOH); 2.5 (m, 1H, H-12). ^{13}C-nmr (75 MHz-$CDCl_3$): 179.7 (COOH); 32.9 (C-12). **7** :$[\alpha]_D^{23}$= +39 (c=0.56, $CHCl_3$); IR: 1740 ($COOCH_3$); ^{1}H-nmr (200 MHz-$CDCl_3$): 3.6 (s,3H, $COOCH_3$), 2.4 and 2.15 (2 m , 2H, H-12 / H-12'); ^{13}C-nmr (75 MHz- $CDCl_3$): 174.3 ($COOCH_3$); 32.9 (C-12).
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(*Received in France* 3 *April* 1996; *accepted* 10 *May* 1996)