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# PHEROMONE SYNTHESIS. PREPARATION OF ERYTHRO-3,7-DIMETHYLPENTADECAN-2-OL, THE ALCOHOL FROM PINE SAWFLY SEX ATTRACTANT (HYMENOPTERA: DIPRIONIDAE).

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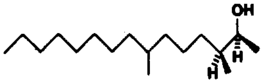
Simple esters (e.g. acetate) of *erythro*-3,7-dimethylpentadecan-2-ol (1) are major components of the sex attractant of several species of pine saw-flies (e.g. *Neodiprion sertifer*, *Diprion similis*; *Hymenoptera*: *Diprionidae*)[1]. The stereostructure at C-7 was not reported (and is possibly of minor importance for receptor recognition). The C-2:C-3 *erythro* structure was determined from



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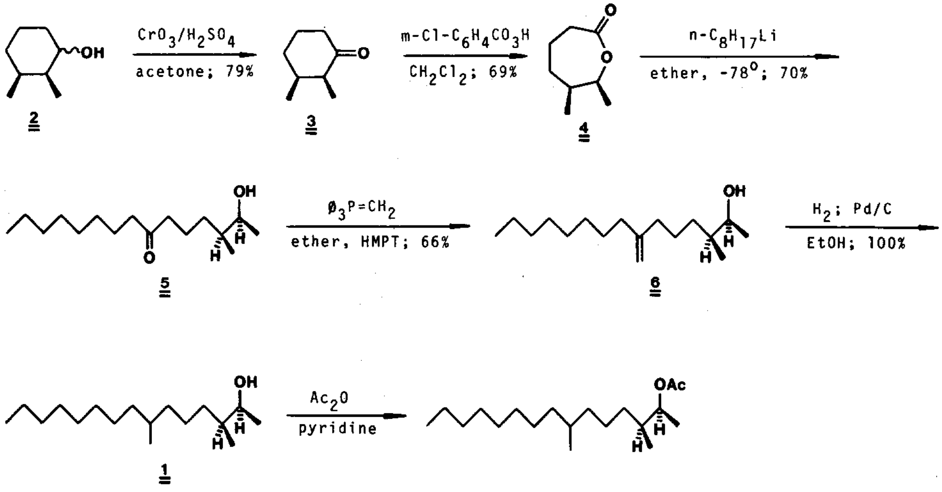
the NMR spectra of natural and synthetic (mixed diastereomeric) esters by consideration of the relative amounts of 1 and its *threo* isomer formed on reaction of methyl magnesium bromide with 2,6-dimethyltetradecanal. This assignment has been confirmed by the present work.

In connection with work[2] on pheromone activities with European species of pine saw-flies, we now report a stereospecific synthesis of compound 1. The method is flexible and permits preparation of both the *erythro* (1) and *threo* isomers and of homologues with different chain lengths.

Commercial[3] 2,3-dimethylcyclohexanol was separated by distillation into two fractions. Jones oxidation of the lowest-boiling fraction (a single compound by GLC) gave pure *trans*-2,3-dimethylcyclohexanone[4]. The second fraction was a mixture of the two *cis*-2,3-dimethylcyclohexanols (2) and gave pure *cis*-2,3-dimethylcyclohexanone[4] (3) in 79% yield on Jones oxidation. Bayer-Villiger oxidation of 3 with m-chloroperbenzoic acid in methylene chloride at 20°C gave practically pure (GLC[5], $^{1}$H- and $^{13}$C-NMR) lactone 4[6]. The lactone was opened with octyllithium to give the hydroxy ketone 5[7]. A modified Wittig reaction[8] of 5 with methylenetriphenylphosphorane gave the olefinic alcohol 6. Catalytic hydrogenation of 6 in ethanol with Pd/C as catalyst gave the alcohol 1[9] in quantitative yield. The over-all yield of 1 from 2 was 25%. The acetate[10] was prepared for comparison with the natural compound (literature data[1]). The $^{1}$H-NMR spectrum of an *erythro*-*threo* mixture of acetates (prepared from a mixture of *cis*- and *trans*-2,3-dimethylcyclohexanone) showed a pair of methyl-group doublets (δ 1.09 and 1.06 ppm; benzene-$d_6$) as reported in reference 1. This confirms the *erythro* configuration of the natural compound.



Synthetic work on the *threo* isomer of 1 and of analogs differing in chain length etc. is in progress.

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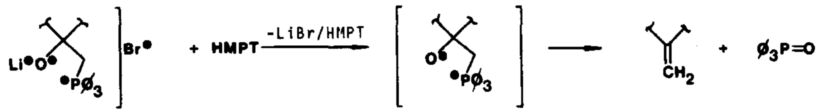
## References and notes

1. D. M. Jewett, F. Matsumura and H. C. Coppel, *Science*, **192**, 51 (1976). These workers also suggest that the active principle in some of the species investigated is one of the optical isomers of 1 (possibly a C-7 diastereomer).
2. Joint project with Dr. J. Löfqvist, Lund (Entomology), Professor T. Norin,

Stockholm (Organic Chemistry) and Dr. G. Bergström, Gothenburg (Ecological Chemistry).

3. Fluka AG, CH-9470 Buchs, Switzerland. See also reference 4.
4. H. E. Ulery and J. H. Richards, J. Amer. Chem. Soc., 86, 3113 (1964).
5. All GLC was performed on a 50 m SE-30 glass capillary column.
6. Yield: 69%; Bp$_{0.11}$: 59-60$^{\circ}$; IR: 1730 cm$^{-1}$; $^{1}$H-NMR (CDCl$_3$) δ 4.61 (1 H, quartet, J=6.5 Hz), 1.33 (3 H, doublet, J=6.5 Hz), 0.94 ppm (3 H, doublet, J=6.5 Hz); $^{13}$C-NMR (CDCl$_3$, TMS) 175.6, 78.1, 36.0, 35.0, 34.7, 20.0, 17.9, 10.3 ppm. Dreiding models of 4 showed that in the stable conformation(s), the dihedral angle between the hydrogen atoms on C-5 and C-6 is close to 90$^{\circ}$ which should, according to the Karplus equation, give a H$_{5-6}$ coupling constant close to 0 Hz. This corroborates the cis-dimethyl assignment in 4.
7. Yield: 70%; Bp$_{0.2}$: 139-140$^{\circ}$; IR: 3440, 1716 cm$^{-1}$; $^{1}$H-NMR (CDCl$_3$) δ 3.71 ppm (1 H, doublet of quartets, J=6.1 and 3.6 Hz); MS, m/e: 256 (M$^{+}$), 238.
8. The hydroxy ketone 5 was added to an ethereal solution containing three equivalents of methylenetriphenylphosphorane (from methyltriphenylphosphonium bromide and n-butyllithium). The mixture was stirred for 15 min. and hexamethylphosphoric triamide (HMPT; three equivalents) was added as a lithium cation-complexing agent in order to accelerate the formation of olefin from the betaine-lithium bromide complex. This dissolved within ca 60 min. and a lithium bromide-HMPT complex separated[*]. {Schlosser and Christmann (Annalen, 708, 1 (1967)) used 1.1 equivalents of a t-BuOK: t-BuOH complex in order to substitute the firmly bound lithium ion for potassium ion in the betaine-lithium halide complex, and thus increase the yields in Wittig reactions}. Stirring overnight at room temperature followed by acidic work-up and column chromatography gave the pure hydroxy-olefin 6: Yield: 66%; IR: 3360, 3078, 1647, 890 cm$^{-1}$; $^{1}$H-NMR (CDCl$_3$) δ 4.68 (2 H, broad singlet, =CH$_2$), 3.68 ppm (1 H, doublet of quartets, J=6.2 and 3.3 Hz); MS, m/e: 254 (M$^{+}$), 236. In a run in which the HMPT-addition was omitted, only 24% yield of 6 was obtained.



[*] In connection with previous work with LiBr/HMPT (G. Magnusson and S. Thorén, J. Org. Chem., 38, 1380 (1973)) we noticed that the complex is rather insoluble in diethyl ether. On addition of HMPT (3 mmol) to a slurry of LiBr (3 mmol) in dry diethyl ether (25 ml), the LiBr first dissolves and after a few minutes a precipitate forms: colourless, hygroscopic crystals: Mp: 77-78$^{\circ}$C; NMR (D$_2$O) shows only HMPT signals. It thus seems probable that on addition of HMPT, the Wittig reaction mixture becomes essentially "salt-free". This is known to greatly enhance the yield and rate in Wittig reac-

tions (Schlosser and Christmann, see above).

9. Probably a C-7 diastereomeric mixture. IR: 3360, 1465, 1379 $cm^{-1}$; $^1H$-NMR ($CDCl_3$) $\delta$ 3.67 ppm (1 H, multiplet); MS, m/e: 238.
10. Pyridine-acetic anhydride. Chromatography on $SiO_2$ with light petroleum/ ethyl acetate 14/1. IR: 1743, 1465, 1377, 1250, 950 $cm^{-1}$; $^1H$-NMR (benzene-$d_6$) $\delta$ 4.96 (1 H, doublet of quartets, J=6.4 and 4.4 Hz), 1.71 (3 H, singlet, $C\underline{H}_3COO$), 1.09 ppm (3 H, doublet, J=6.45 Hz); $^{13}C$-NMR (benzene-$d_6$, TMS) 169.6, 73.5 ppm, $\underline{C}$=O and -$\underline{C}$H-O- respectively; there were no other peaks in the vicinity, indicating a very high erythro/threo ratio in the product. This also means that the Bayer-Villiger oxidation ($\underline{\underline{3}}\rightarrow\underline{\underline{4}}$) is highly (and probably completely) stereospecific. MS, m/e: 238, 87. The erythro-threo mixture of acetates showed $^{13}C$-NMR peaks at 169.6, 73.9, 73.5 ppm.