Synthesis of derivatives of (*S*)-2-alkanols, components of pheromones of *Drosophila mulleri* and *Rhyzopertha dominica*, from (*S*)-(+)-3,7-dimethylocta-1,6-diene

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Effective routes for the synthesis of (*S*)-2-acetoxytridecane, the sex pheromone of the fruit fly *Drosophila mulleri*, and (*S*)-1-methylbutyl 2-methyl- and 2,4-dimethylpent-2*E*-enoates, components of the aggregation pheromone of the lesser grain borer *Rhyzopertha dominica*, were developed on the basis of (*S*)-4-methylhex-5-en-1-yl tosylate accessible from (*S*)-(+)-dihydromyrcene.

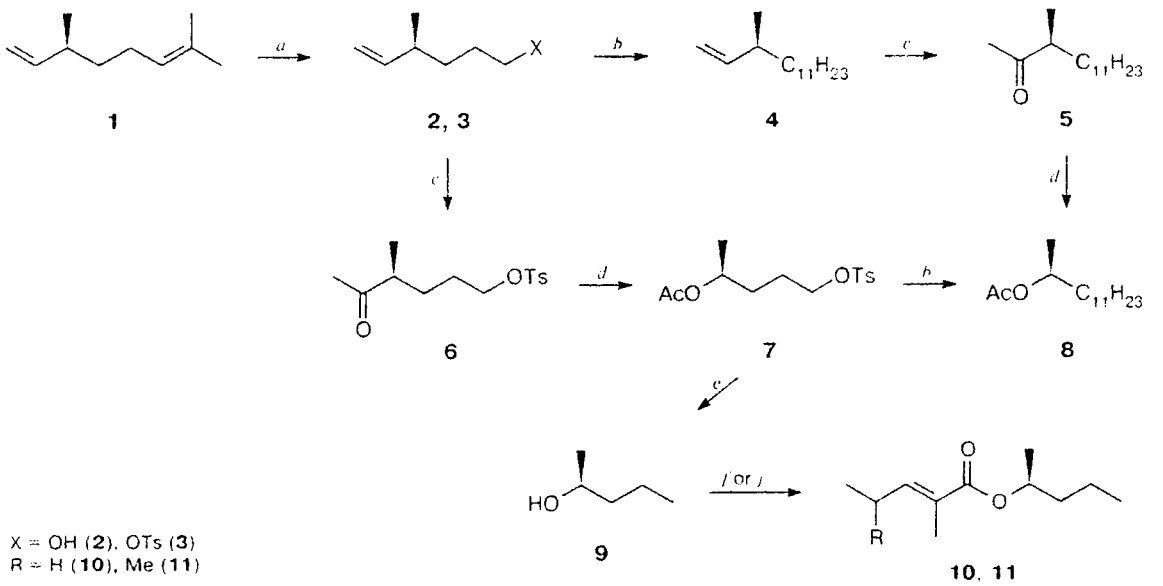
Key words: (*S*)-2-acetoxytridecane, (*S*)-tridec-2-yl acetate, (*S*)-(+)-3,7-dimethylocta-1,6-diene, dominicalur, (*S*)-4-methylhex-5-en-1-ol, (*S*)-pentan-2-ol, cross-coupling, Baeyer—Villiger reaction, Wacker—Tsuji reaction, pheromone.

Previously, selective transformation of enantiomerically enriched (*ee* ~50%) (*S*)-(+)-3,7-dimethylocta-1,6-diene (**1**) into (*S*)-(+)-4-methylhex-5-en-1-ol (**2**) by selective epoxidation[1] or ozonolysis[2] at the trisubstituted double bond and the use of the product in the synthesis of several insect pheromones have been reported.

In this work, we investigated the synthetic potential of unsaturated alcohol **2** based on selective transformations of its tosylate (**3**) in relation to the synthesis of three components of insect pheromones (**8**, **10**, **11**), derivatives of (*S*)-2-alkanols.

One of the approaches that we propose for the preparation of (*S*)-2-acetoxytridecane (**8**), the sex pheromone

Scheme 1



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of the fruit fly (*Drosophila mulleri*), which has been synthesized previously using either enzymatic transformations[3,4] or an enantiodifferentiating SAMP reagent,[5] is based on the catalytic cross-coupling of tosylate **3** with octylmagnesium bromide. In addition to (*S*)-3-methyltetradec-1-ene (**4**), the reaction product thus obtained contained 23% hexadecane, difficult to separate, which resulted from homocoupling of the Grignard reagent and was separated in the next step. Consecutive oxidation by molecular oxygen in the presence of a palladium catalyst, first, of alkene **4** and then of the resulting (*S*)-3-methyltetradecan-2-one (**5**) (Scheme 1) under the conditions of regio- and stereospecific Baeyer—Villiger reaction completed the synthesis of pheromone **8** in an overall yield of 40% based on the starting diene **1**.

An alternative, less effective (overall yield 20%) pathway to chiral acetate **8** consists of oxidative transformation of vinyl tosylate **3** according to Wacker—Tsuji to give ketone **6** and Baeyer—Villiger transformation of **6** into acetoxy tosylate **7**, which is then involved into chemoselective (non involving the acetoxy group) cross-coupling with the magnesiumeuprate reagent generated from *n*-octyl bromide.

The reduction of diester **7** on treatment with $LiAlH_4$ proceeding with retention of the configuration of the chiral center resulted in the synthesis of enantiomerically enriched (*S*)-pentan-2-ol (**9**), which was then readily transformed[8] into dominicalur-1 (**10**) and dominicalur-2 (**11**), which are components of the aggregation pheromone of the lesser grain borer (*Rhyzopertha dominica*).

Experimental

IR spectra were recorded on a UR-20 instrument in thin films. ^1H NMR spectra (δ) were recorded on a Bruker AM-300 spectrometer (operating at 300.13 MHz) in $CDCl_3$ using Me_4Si as the standard. Chromatographic analysis was carried out on a Chrom-5 instrument (column length 1.2 m; silicone SE-30 (5%) on Chromaton N-AW-DMCS (0.16—0.20 mm) as the stationary phase; operating temperature 50—300 °C); helium was used as the carrier gas. Optical rotation was measured on a Perkin-Elmer-241-MC polarimeter. Solvents were dried by standard procedures:[7] THF and Et_2O were distilled from DIBAH prior to the reaction. Commercial samples of chemically pure grade 1-octyl bromide (Erevan plant of chemicals) and $LiAlH_4$ (USSR) were used as received; commercial TsCl (pure grade, Shostka plant of chemicals) was recrystallized from $CHCl_3$; and Li_2CuCl_4 was prepared by a known procedure.[8] Chromatography was carried out on silica gel L (40—100 μm), Chemapol (Czech Republic). TLC monitoring was carried out on SiO_2 (Silufol, Czech Republic) using petroleum ether and a petroleum ether—Et_2O mixture (2 : 1) for elution. Petroleum ether with b.p. 40—70 °C was used for chromatography. Oxidation of ketones **5** and **6** was performed using MCPBA (Fluka), which contained 55% major component according to iodometric titration.

(*S*)-3-Methyltetradecan-2-one (5). Tosylate **3**[1] (*ee* ~50%) (6.28 g, 23.4 mmol) in 37 mL of anhydrous Et_2O was added with stirring (Ar) at −50 °C to a solution of the Grignard reagent prepared from 1-octyl bromide (9.03 g, 46.8 mmol) and Mg (1.25 g, 52.1 mmol) in 47 mL of anhydrous THF. The mixture was cooled to −70 °C, and a 0.2 *M* solution of Li_2CuCl_4 in anhydrous THF (1.17 mL) was added dropwise. The reaction mixture was stirred for 1 h at −70 °C, diluted with 100 mL of Et_2O, and poured into 60 mL of a cold saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×50 mL). The extracts were combined with the organic layer, washed successively with saturated solutions of NH_4Cl and $NaHCO_3$ and with brine, dried with $MgSO_4$, and concentrated to give 5.27 g of a product that contained, according to GLC, 77% olefin **4** and 23% hexadecane. IR, ν/cm^{-1}: 930, 1660 (C=C); 3100 (=CH_2). CuCl (1.90 g, 1.9 mmol) was added at 60 °C to a mixture of $PdCl_2$ (0.34 g, 1.9 mmol), THF (173 mL), and H_2O (19 mL). Then O_2 was passed through the reaction mixture with vigorous stirring for 5 min at a rate of 5 L h^{-1}, the product prepared above (5.20 g) was added, and O_2 was bubbled through the reaction mixture at a rate of 5 L h^{-1} for 6 h (60 °C). The catalyst was filtered off, and the filtrate was diluted with 100 mL of $CHCl_3$, washed with 5% HCl (3×50 mL) saturated with brine, dried with $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 to give 3.45 g of an oily compound **5** (66% based on **3**), $[\alpha]_D^{20}$ +0.55° (*c* 30.0, $CHCl_3$). Found (%): C, 79.69; H, 13.21. $C_{15}H_{30}O$. Calculated (%): C, 79.58; H, 13.36. IR, ν/cm^{-1}: 1712 (C=O). ^1H NMR: 0.81 (t, 3 H, H(14), J = 6.8 Hz); 0.99 (d, 3 H, MeC(3), J = 6.7 Hz); 1.18 (m, 20 H, CH_2); 2.06 (s, 3 H, H(1)); 2.39—2.50 (m, 1 H, H(3)).

(*S*)-4-Methyl-5-oxohex-1-yl tosylate (6). Oxygen was bubbled at a rate of 5 L h^{-1} for 1 h through a mixture of $PdCl_2$ (0.50 g, 2.8 mmol), CuCl (2.68 g, 27.1 mmol), DMF (14 mL), and H_2O (1.8 mL) stirred at 22 °C. Tosylate **3** (6.52 g, 24.3 mmol) as an oil was added and O_2 was passed at a rate of 5 L h^{-1} for 12 h. After the reaction was over (TLC monitoring), 10% HCl (8 mL) was added, the mixture was stirred for 1 h and extracted with Et_2O (4×50 mL), and the extract was washed successively with H_2O, with a saturated solution of $NaHCO_3$, and with brine and dried with Na_2SO_4. Evaporation of the solvent gave 4.56 g (66%) of keto tosylate **6**. IR, ν/cm^{-1}: 1052 (H_2C—O); 1176, 1356 (S=O); 1596 (Ar); 1712 (C=O). ^1H NMR: 1.07 (d, 3 H, MeC(4), J = 7.0 Hz); 1.30—1.50 (m, 1 H, H(4)); 1.53—1.73 (m, 4 H, H(2), H(3)); 2.12 (s, 3 H, H(6)); 2.43 (s, 3 H, Me—Ar); 4.00 (t, 2 H, H(1), J = 6.2 Hz); 7.36 and 7.79 (both d, 4 H, H—Ar, J = 8.0 Hz).

(*S*)-5-Tosyloxypent-2-yl acetate (7). A solution of tosylate **6** (4.40 g, 15.5 mmol) in 7 mL of $CHCl_3$ was added dropwise over a period of 10 min (0 °C) to a stirred suspension of MCPBA (5.24 g, 16.7 mmol) in 20 mL of anhydrous $CHCl_3$. The mixture was stirred for 24 h at ~20 °C, diluted with 200 mL of Et_2O, washed successively with a 5% solution of Na_2SO_3, a saturated solution of $NaHCO_3$ and with brine, and dried with $MgSO_4$. Evaporation of the solvent gave 3.16 g (68%) of diester **7** as an oil. IR, ν/cm^{-1}: 1045 (H_2C—O); 1176, 1356 (S=O); 1250 (O—C—O); 1610 (Ar); 1735 (C=O). ^1H NMR: 1.18 (d, 3 H, C(1)H_3, J = 6.0 Hz); 1.51—1.75 (m, 4 H, H(3), H(4)); 2.00 (s, 3 H, $MeCO_2$); 2.45 (s, 3 H, Me—Ar); 4.03 (t, 2 H, H(5), J = 6.0 Hz); 4.79—4.90 (m, 1 H, H(2)); 7.36 and 7.79 (both d, 4 H, H—Ar, J = 8.0 Hz).

(*S*)-Tridec-2-yl acetate (8). *A.* Ketone **5** (3.00 g, 13.3 mmol) in 5 mL of $CHCl_3$ was added dropwise to a suspension of MCPBA (4.55 g, 14.5 mmol) in 20 mL of anhydrous $CHCl_3$ at ~20 °C. The reaction mixture was stirred for 8 h at ~20 °C, diluted with 200 mL of Et_2O, washed successively with a 5% solution of Na_2SO_3, a saturated solution of $NaHCO_3$ and with brine, dried with $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 to give 3.81 g (82%) of acetate **8** as an oil, $[\alpha]_D^{21}$ +2.12° (*c* 0.25,

hexane); *cf.* Ref. 5: $[\alpha]_D^{23}$ +4.31° (*c* 0.31, hexane). The ^{1}H NMR and IR spectra were identical to those described previously.[5]

B. A solution of tosylate **7** (1.30 g, 4.3 mmol) in 7 mL of anhydrous THF was added dropwise with stirring at −75 °C (Ar) to a solution of the Grignard reagent prepared from *n*-octyl bromide (1.19 g, 6.2 mmol) and Mg (0.16 g, 6.7 mmol) in 6 mL of anhydrous Et_2O. Then a 0.2 *M* solution of Li_2CuCl_4 in THF (0.24 mL) was added. The reaction mixture was stirred (−70 °C, 1 h; −10 °C, 2 h; 25 °C, 2 h), poured into a cooled solution of NH_4Cl, and extracted with Et_2O (3×50 mL). The combined extract was washed successively with brine, a saturated solution of $NaHCO_3$, and again with brine, dried with $MgSO_4$, and concentrated. The residue was chromatographed on SiO_2 to give 0.60 g (58%) of acetate **8** identical to that obtained by procedure ***A***.

(*S*)-Pentan-2-ol (9). $LiAlH_4$ (0.14 g, 3.7 mmol) was added with stirring (0 °C, Ar) to a solution of acetoxytosylate **7** (1.00 g, 3.3 mmol) in 20 mL of anhydrous Et_2O. The reaction mixture was stirred for 4 h at 0 °C, H_2O (0.2 mL) was added, the temperature was raised to ~20 °C, the mixture was stirred for 3 h, and the precipitate was filtered off and washed with 50 mL of Et_2O. The combined filtrate was dried with Na_2SO_4 and concentrated to give 0.23 g (79%) of alcohol **9**. $[\alpha]_D^{23}$ +5.42° (*c* 3, $CHCl_3$); *cf.* Ref. 6: $[\alpha]_D^{28}$ +11.34° (*c* 5, $CHCl_3$). The ^{1}H NMR spectral parameters were identical to those described previously.[6]

(*S*)-1-Methylbutyl 2-methylpent-2*E*-enoate (10) was prepared by a procedure described previously[6] from alcohol **9** (0.50 g, 5.7 mmol), 2-methylpent-2*E*-enoyl chloride[6] (0.65 g, 4.9 mmol), and Py (3.2 mL) in 1.6 mL of Et_2O. The reaction gave 0.98 g (94%) of ester **10**. $[\alpha]_D^{23}$ +15.1° (*c* 2, $CHCl_3$); *cf.* Ref. 6: $[\alpha]_D^{24}$ +30.14° (*c* 4, $CHCl_3$). The ^{1}H NMR spectral parameters were identical to those described previously.[6]

(*S*)-1-Methylbutyl 2,4-dimethylpent-2*E*-enoate (11) was prepared by a procedure described previously[8] from alcohol **10** (0.50 g, 5.7 mmol), 2,4-dimethylpent-2*E*-enoyl chloride[6] (0.64 g, 4.4 mmol), and Py (3.2 mL) in 1.6 mL of Et_2O. This gave 1.07 g (95%) of ester **11**. $[\alpha]_D^{23}$ +15.3° (*c* 3, $CHCl_3$); *cf.* Ref. 6: $[\alpha]_D^{28}$ +32.95° (*c* 3, $CHCl_3$). The ^{1}H NMR spectral parameters were identical to those described previously.[6]

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References

1. Nguen Kong Khao, M. V. Mavrov, and E. P. Serebryakov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, 693 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37** (Engl. Transl.)].
2. V. N. Odinokov, O. C. Kukovinets, V. G. Kasradze, A. V. Dolidze, V. R. Akhmetova, E. P. Cerebryakov, and G. A. Toistikov, *Zh. Org. Khim.*, 1993, **29**, 39 [*J. Org. Chem.*, 1993, **29** (Engl. Transl.)].
3. Y. Naoshima, M. Kamezawa, H. Tachibana, Y. Munakata, T. Fujita, K. Kihara, and T. Raku, *J. Chem. Soc., Perkin Trans. 1*, 1993, 557.
4. A. S. Gopalan and H. K. Jacobs, *Tetrahedron Lett.*, 1990, **39**, 5575.
5. D. Enders and A. Plant, *Liebigs Ann. Chem.*, 1991, 1241.
6. B. A. Cheskis, N. A. Shpiro, and A. M. Moiseenkov, *Zh. Org. Khim.*, 1990, **26**, 1864 [*J. Org. Chem.*, 1990, **26** (Engl. Transl.)].
7. A. Gordon and R. Ford, *The Chemist's Companion. A Handbook of Practical Data, Techniques, and References*, Wiley, New York, 1972.
8. G. A. Tolstikov, V. N. Odinokov, G. Yu. Ishmuratov, R. I. Galeeva, and G. G. Balezina, *Khim. Prirodn. Soedinenii*, 1982, 750 [*Chem. Nat. Comp.*, 1982 (Engl. Transl.)].

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